



US009150507B2

(12) **United States Patent**
Okuno et al.

(10) **Patent No.:** US 9,150,507 B2
(45) **Date of Patent:** *Oct. 6, 2015

(54) **AMINE DERIVATIVE HAVING NPY Y5 RECEPTOR ANTAGONISTIC ACTIVITY**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 745 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **12/226,516**

(22) PCT Filed: **Apr. 25, 2007**

(86) PCT No.: **PCT/JP2007/058938**

§ 371 (c)(1),
(2), (4) Date: **Oct. 21, 2008**

(87) PCT Pub. No.: **WO2007/125952**

PCT Pub. Date: **Nov. 8, 2007**

(65) **Prior Publication Data**

US 2010/0063027 A1 Mar. 11, 2010

(30) **Foreign Application Priority Data**

Apr. 28, 2006 (JP)	2006-124762
Aug. 11, 2006 (JP)	2006-219606
Feb. 26, 2007 (JP)	2007-045587

(51) **Int. Cl.**

C07C 311/05	(2006.01)
C07C 311/07	(2006.01)

(Continued)

(52) **U.S. Cl.**

CPC	C07C 311/05 (2013.01); C07C 311/07 (2013.01); C07C 311/08 (2013.01); C07C 311/20 (2013.01); C07C 311/21 (2013.01); C07C 311/37 (2013.01); C07C 311/39 (2013.01); C07C 311/43 (2013.01); C07C 317/36 (2013.01); C07D 207/27 (2013.01); C07D 207/325 (2013.01); C07D 211/14 (2013.01); C07D 213/38 (2013.01); C07D 213/74 (2013.01); C07D 213/82 (2013.01); C07D 215/38 (2013.01); C07D 217/04 (2013.01); C07D 217/14 (2013.01); C07D 217/22 (2013.01); C07D 219/10 (2013.01); C07D 231/38 (2013.01); C07D 233/58 (2013.01); C07D 233/61 (2013.01); C07D 235/30 (2013.01); C07D 237/20 (2013.01); C07D 237/22 (2013.01); C07D 237/34 (2013.01); C07D 239/42 (2013.01); C07D 241/20 (2013.01); C07D 261/14 (2013.01); C07D 261/20 (2013.01); C07D 263/58 (2013.01); C07D 265/30 (2013.01); C07D 265/36 (2013.01); C07D 267/14 (2013.01);
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C07D 275/02 (2013.01); **C07D 277/28** (2013.01); **C07D 277/62** (2013.01); **C07D 277/82** (2013.01); **C07D 295/12** (2013.01); **C07D 295/135** (2013.01); **C07D 295/18** (2013.01); **C07D 333/36** (2013.01); **C07D 333/40** (2013.01); **C07D 333/66** (2013.01); **C07D 333/72** (2013.01); **C07D 403/04** (2013.01); **C07D 409/04** (2013.01); **C07D 413/04** (2013.01); **C07D 417/12** (2013.01); **C07D 498/04** (2013.01); **C07D 513/04** (2013.01); **C07C 2101/02** (2013.01); **C07C 2101/04** (2013.01); **C07C 2101/08** (2013.01); **C07C 2101/14** (2013.01); **C07C 2102/08** (2013.01); **C07C 2102/10** (2013.01); **C07C 2103/18** (2013.01)

(58) **Field of Classification Search**

CPC C07C 311/05
See application file for complete search history.

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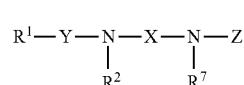
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Primary Examiner — Paul Zarek

(74) Attorney, Agent, or Firm — Oblon, McClelland, Maier & Neustadt, L.L.P.

(57) **ABSTRACT**

This invention provides a compound of the formula (I):



a pharmaceutically acceptable salt or solvate thereof,
wherein

R¹ is optionally substituted lower alkyl,

Y is —S(O)_n— wherein n is 1 or 2, or —CO—,

R² is hydrogen or lower alkyl,

R⁷ is hydrogen or lower alkyl,

X is lower alkylene, lower alkenylene, arylene, cycloalkylene or the like, and

Z is lower alkyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl or the like.

10 Claims, No Drawings

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**AMINE DERIVATIVE HAVING NPY Y5
RECEPTOR ANTAGONISTIC ACTIVITY****FIELD OF THE INVENTION**

This invention relates to a new compound having NPY Y5 receptor antagonistic activity. The compound is useful as a pharmaceutical composition, especially an anti-obesity agent.

BACKGROUND ART

Neuropeptide Y (hereinafter referred to as NPY) is a peptide which consists of 36 amino acid residues and was isolated from porcine brain in 1982. NPY is widely distributed in the central nervous system and peripheral tissues of humans and animals.

It has been reported that NPY possesses a stimulating activity of food intake, an anti-seizure activity, a learning-promoting activity, an anti-anxiety activity, an anti-stress activity etc. in central nervous system, and it may be pivotally involved in the central nervous system diseases such as depression, Alzheimer's disease and Parkinson's disease. NPY is thought to be associated with the cardiovascular diseases, since it induces a contraction of smooth muscles such as blood vessels or cardiac muscles in the peripheral tissues. Furthermore, NPY is also known to be involved in the metabolic diseases such as obesity, diabetes and hormone abnormalities (Non-patent Document 1). Therefore, an NPY receptor antagonist is expected as a medicine for preventing or treating various diseases involved in the NPY receptor like the above.

Subtypes of Y1, Y2, Y3, Y4, Y5, and Y6 have now been identified as the NPY receptor (Non-patent Document 2). It has been suggested that the Y5 receptor is at least involved in the feeding behavior and its antagonist is expected as an anti-obesity agent (Non-patent Document 3).

Amine derivatives having sulfonyl group and similar structures to compounds of the present invention and exhibiting NPY Y5 receptor antagonistic activity are disclosed in Patent Document 1, 2, 3, 4 and the like. Amide derivatives having sulfonyl group and exhibiting NPY Y5 receptor antagonistic activity are disclosed in Patent Document 5, 8, 9, 10 and 11. Derivatives having sulfonyl group and exhibiting NPY Y5 receptor antagonistic activity are disclosed in Patent Document 12. The structures of these compounds are different from those of the compounds of the present invention.

Furthermore, although compounds having similar structures to compounds of the present invention are disclosed in Patent Document 6, 7, 13, 14 and the like, the activities of their compounds are quite different from those of the compounds of the present invention and these documents do not suggest the present invention.

[Non-patent Document 1] Trends in Pharmacological Sciences, Vol. 15, 153(1994)

[Non-patent Document 2] Trends in Pharmacological Sciences, Vol. 18, 372(1997)

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- [Patent Document 10] WO2007/002126
- [Patent Document 11] WO2006/001318
- [Patent Document 12] WO2005/080348
- [Patent Document 13] US2007/060598
- [Patent Document 14] WO2005/121107

DISCLOSURE OF INVENTION10 **Problems to be Solved by the Invention**

The object of the present invention is to provide excellent new compounds having NPY Y5 receptor antagonistic activity. In our examination, compounds in Patent Document 1 or 15 2 showed the strong induction of a drug-metabolizing enzyme and some compounds in Patent Document 10 showed toxicity such as anemia induction.

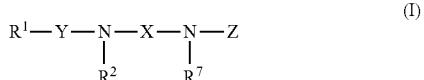
20 **Means for Solving the Problem**

The present inventors have intensively studied to synthesize the following excellent new compounds having NPY Y5 receptor antagonistic activity. Patent Document 5 disclosed that amide derivatives having sulfonyl group are compounds having NPY Y5 receptor antagonistic activity. However, the present inventors found that transportability of compounds which the amide is substituted with the amine through the blood-brain barrier is much higher than that of the unsubstituted compounds. Furthermore, the inventors found that compounds of the present invention have less the induction of a drug-metabolizing enzyme compared to compounds described in Patent Document 1 or 2 to achieve the present invention.

The present invention includes the followings.

35 (1) A compound of the formula (I):

40 [Formula 1]



45 a pharmaceutically acceptable salt or solvate thereof, wherein

R1 is optionally substituted lower alkyl,

Y is $-\text{S}(\text{O})\text{n}-$ wherein n is 1 or 2, or $-\text{CO}-$,

50 R2 is hydrogen or optionally substituted lower alkyl,

R1 and R2 taken together may form lower alkylene,

R7 is hydrogen or optionally substituted lower alkyl,

X is optionally substituted lower alkylene,

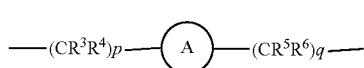
optionally substituted lower alkenylene,

optionally substituted $-\text{CO}-$ lower alkylene,

optionally substituted $-\text{CO}-$ lower alkenylene or

a group of the formula:

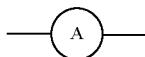
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[Formula 2]

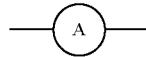
65 wherein R3, R4, R5 and R6 are each independently hydrogen or optionally substituted lower alkyl,

a group of the formula:



[Formula 3]

wherein a group of the formula:



[Formula 9]

is optionally substituted cycloalkylene, optionally substituted cycloalkenylene, optionally substituted bicycloalkylene, optionally substituted arylene or optionally substituted heterocyclidyl,

p and q are each independently an integer between 0 and 2, either p or q is not 0, and provided that a group of the formula:



[Formula 4]

is optionally substituted cycloalkylene, p is 0, q is 1 and Z is optionally substituted pyrimidinyl is excluded.

(2) The compound, pharmaceutically acceptable salt or solvate thereof of (1), wherein R1 is lower alkyl.

(3) The compound, pharmaceutically acceptable salt or solvate thereof of (1), wherein Y is S(O)2- .

(4) The compound, pharmaceutically acceptable salt or solvate thereof of (1), wherein Z is optionally substituted carbocycl or optionally substituted heterocycl.

(5) The compound, pharmaceutically acceptable salt or solvate thereof of (1), wherein X is a group of the formula:

is not a group of the formula:



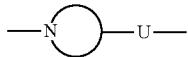
[Formula 5]

and

R1 is optionally substituted C2 to C10 alkyl.

(6) The compound, pharmaceutically acceptable salt or solvate thereof of (5), wherein Z is optionally substituted heterocycl.

(7) The compound, pharmaceutically acceptable salt or solvate thereof of (5), wherein a group of the formula:



[Formula 6]

wherein a group of the formula:



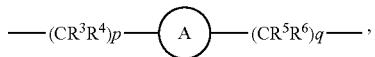
[Formula 7]

is piperidinediyl, piperazinediyl, pyridindiy, pyrazinediyl, pyrrolidinediyl or pyrrolediyl, and U is lower alkylene or lower alkenylene,

Z is optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted amino, optionally substituted lower alkoxy, optionally substituted carbocycl or optionally substituted heterocycl,

provided that Z is not fused heterocycl consisting of three rings, optionally substituted thiazoly or optionally substituted quinazolinyl, and

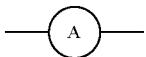
provided that a compound wherein X is a group of the formula:



[Formula 8]

is optionally substituted cycloalkylene, optionally substituted cycloalkenylene, optionally substituted bicycloalkylene or optionally substituted piperidinylene.

(8) The compound, pharmaceutically acceptable salt or solvate thereof of (5), wherein a group of the formula:



[Formula 11]

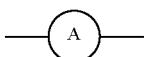
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is optionally substituted cyclohexylene or optionally substituted piperidinylene,

p and q are each independently 0 or 1, either p or q is not 0.

(9) The compound, pharmaceutically acceptable salt or solvate thereof of (7) or (8), wherein Z is optionally substituted lower alkyl, optionally substituted phenyl, optionally substituted pyridyl, optionally substituted pyrazolyl, optionally substituted isoxazolyl, optionally substituted oxadiazolyl, optionally substituted pyridazinyl, optionally substituted pyrazinyl, optionally substituted pyrimidinyl or optionally substituted fused heterocycl consisting of two rings.

(10) The compound, pharmaceutically acceptable salt or solvate thereof of (1), wherein X is a group of the formula:



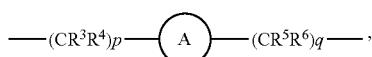
[Formula 12]

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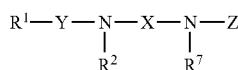
and

p+q is 1 or 2.

(11) The compound, pharmaceutically acceptable salt or solvate thereof of (10), wherein p+q is 1.

(12) A compound of the formula (I):

[Formula 14]



a pharmaceutically acceptable salt or solvate thereof, wherein

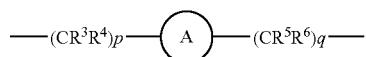
R1 is optionally substituted lower alkyl,

Y is —S(O)2-,

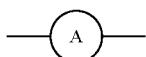
R2 is hydrogen or optionally substituted lower alkyl,

R7 is hydrogen or optionally substituted lower alkyl,

X is a group of the formula:



wherein R5 and R6 are each independently hydrogen, a group of the formula:



is optionally substituted cycloalkylene,

p is 0, and

q is 1 or 2,

Z is optionally substituted carbocyclyl or optionally substituted heterocyclyl, and provided that a compound wherein Z is fused heterocyclyl consisting of three rings or optionally substituted pyrimidinyl is excluded.

(13) The compound, pharmaceutically acceptable salt or solvate thereof of (12), wherein Z is optionally substituted phenyl, optionally substituted indanyl, optionally substituted pyridyl, optionally substituted pyridazinyl, optionally substituted pyrimidinyl, optionally substituted pyrazolyl, optionally substituted isoxazolyl, optionally substituted oxadiazolyl or optionally substituted fused heterocyclyl consisting of two rings.

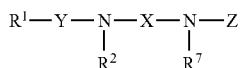
(14) The compound, pharmaceutically acceptable salt or solvate thereof of (12), wherein Z is optionally substituted isoquinolyl, optionally substituted benzothiazolyl, optionally substituted benzoxazolyl, optionally substituted benzopyridyl, optionally substituted benzopyridazinyl, optionally substituted benzimidazolyl, optionally substituted thiazolopyridyl, optionally substituted benzisoxazolinonyl, optionally substituted benzoxazolinonyl, optionally substituted benzoxadionyl or optionally substituted benzoxyazepinonyl.

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(15) A compound of the formula (I):

[Formula 17]

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10 a pharmaceutically acceptable salt or solvate thereof, wherein

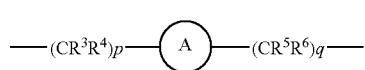
R1 is optionally substituted lower alkyl,

Y is —S(O)2-,

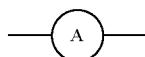
R2 is hydrogen or optionally substituted lower alkyl,

R7 is hydrogen or optionally substituted lower alkyl,

X is a group of the formula:



20 wherein R3 and R4 are each independently hydrogen, a group of the formula:

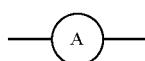


is optionally substituted cycloalkylene,

p is 1 or 2, and

q is 0,

provided that



40 is not



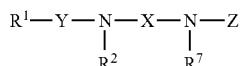
wherein R14 is optionally substituted phenyl,

Z is optionally substituted carbocyclyl or optionally substituted heterocyclyl, and provided that a compound wherein Z is fused heterocyclyl consisting of three rings, optionally substituted thiazolyl or optionally substituted quinazolinyl is excluded.

45 (16) The compound, pharmaceutically acceptable salt or solvate thereof of (15), wherein Z is optionally substituted phenyl, optionally substituted pyridyl, optionally substituted pyridazinyl, optionally substituted pyrazinyl, optionally substituted pyrimidinyl, optionally substituted quinolyl, optionally substituted isoquinolyl, optionally substituted benzothiazolyl, 50 optionally substituted benzimidazolyl, optionally substituted benzoxazolyl, 55 optionally substituted thiazolopyridyl or optionally substituted oxazolopyridyl.

(17) A compound of the formula (I):

[Formula 22]



a pharmaceutically acceptable salt or solvate thereof,
wherein

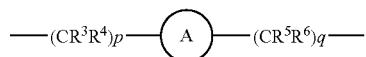
R1 is optionally substituted lower alkyl,

Y is $-S(O)2-$,

R2 is hydrogen or optionally substituted lower alkyl,

R7 is hydrogen or optionally substituted lower alkyl,

X is a group of the formula:



[Formula 23]

wherein R3 and R4 are each independently hydrogen,
a group of the formula:



[Formula 24]

is optionally substituted cycloalkylene,

p is 1 or 2, and

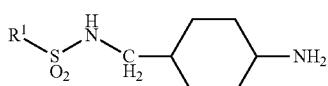
q is 0, and

Z is optionally substituted phenyl, optionally substituted pyridyl, optionally substituted pyridazinyl, optionally substituted pyrazinyl, optionally substituted pyrimidinyl, optionally substituted quinolyl, optionally substituted isoquinolyl, optionally substituted benzothiazolyl, optionally substituted benzimidazolyl, optionally substituted benzoxazolyl, optionally substituted thiazolopyridyl or optionally substituted oxazolopyridyl.

(18) A pharmaceutical composition comprising the compound, pharmaceutically acceptable salt or solvate thereof of any one of (1) to (17) as an active ingredient.

(19) A NPY Y5 receptor antagonist comprising the compound, pharmaceutically acceptable salt or solvate thereof of any one of (1) to (17) as an active ingredient.

(20) A compound of the formula:



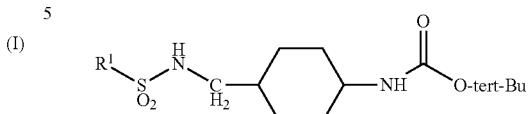
[Formula 25]

a salt or solvate thereof,

wherein R1 is ethyl or tert-butyl.

(21) A compound of the formula:

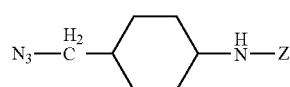
[Formula 26]



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a salt or solvate thereof,
wherein R1 is ethyl, isopropyl or tert-butyl.

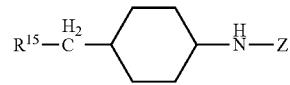
(22) A compound of the formula:



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a salt or solvate thereof,
wherein Z is optionally substituted carbocyclyl or optionally substituted heterocyclyl.

(23) A compound of the formula:



[Formula 28]

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a salt or solvate thereof,
wherein

R15 is NH2 or OH, and

35 Z is optionally substituted pyridyl, optionally substituted pyridazinyl, optionally substituted pyrazinyl, optionally substituted pyrimidinyl, optionally substituted quinolyl, optionally substituted isoquinolyl, optionally substituted benzothiazolyl, optionally substituted benzoxazolyl, optionally substituted benzopyridyl, optionally substituted benzopyridazinyl, optionally substituted benzimidazolyl, optionally substituted benzoxazolyl, optionally substituted thiazolopyridyl or optionally substituted benzisoxazolinonyl, optionally substituted benzoxazolinonyl, optionally substituted benzoxadionyl or optionally substituted benzoxyazepinonyl.

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Effect of the Invention

A compound of the present invention exhibits NPY Y5 receptor antagonistic activity and are very useful as a medicine especially for preventing and/or treating feeding disorder, obesity, hyperorexia, sexual disorder, impaired fertility, depression, epileptic seizure, hypertension, cerebral hemorrhage, congestive heart failure or sleep disorders.

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BEST MODE FOR CARRYING OUT THE INVENTION

Each term used in this description is explained below. The each term has the same meaning in this description both when it is used alone each term and when it is used with the other term.

The term "halogen" includes fluorine, chlorine, bromine and iodine. Especially, fluorine or chlorine is preferable.

65 The term "protective group" in "optionally protected hydroxyl" and "optionally protected hydroxy lower alkyl" includes all of hydroxy protecting groups usually used. For example, acyl such as acetyl, trichloroacetyl and benzoyl,

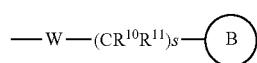
lower alkoxy carbonyl such as t-butoxycarbonyl, lower alkylsulfonyl such as methane sulfonyl, lower alkoxy(lower)alkyl such as methoxymethyl and trialkylsilyl such as t-butyldimethylsilyl are included.

The term "lower alkyl" includes C1 to C10 straight or branched alkyl. Examples are methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, isopenetyl, neopentyl, hexyl, isoheptyl, n-heptyl, isoheptyl, n-octyl, isooctyl, n-nonyl, n-decyl and the like.

"Lower alkyl" represented by R¹ is preferably C2 to C10, more preferably C2 to C6 alkyl and most preferably ethyl, isopropyl or t-butyl.

"Lower alkyl" in other cases is preferably C1 to C6 and more preferably C1 to C4 alkyl.

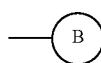
The examples of substituents of "optionally substituted lower alkyl" represented by Z are, (1) halogen; (2) cyano; (3) the following groups (i) to (xvi), which are optionally substituted with one or more substituents selected from "a substituents group β" defined below, (i) hydroxy, (ii) lower alkoxy, (iii) mercapto, (iv) lower alkylthio, (v) acyl, (vi) acyloxy, (vii) carboxy, (viii) lower alkoxy carbonyl, (ix) imino, (x) carbamoyl, (xi) thiocarbamoyl, (xii) lower alkylcarbamoyl, (xiii) lower alkylthiocarbamoyl, (xiv) amino, (xv) lower alkylamino or (xvi) heterocyclcarbonyl; or (4) a group of the formula:



[Formula 29]

wherein R¹⁰ and R¹¹ are each independently hydrogen or lower alkyl and when this group has two or more of R¹⁰ and/or two or more of R¹¹, each R¹⁰ and/or each R¹¹ may be different.

W is single bond, O, S or NR¹², R¹² is hydrogen, lower alkyl or phenyl, a group of the formula:



[Formula 30]

is cycloalkyl, bicycloalkyl, cycloalkenyl, aryl or heterocycl, each of which is optionally substituted with one or more of substituents selected from "a substituents group α" defined below and

s is an integer of 0 to 4.

In the present specification, "a substituents group α" is a group constituting of (1) halogen; (2) oxo; (3) cyano; (4) nitro; (5) imino optionally substituted with lower alkyl or hydroxy;

(6) the following groups (i) to (xxi), which are optionally substituted with one or more of groups selected from the substituents group β,

(i) hydroxy, (ii) lower alkyl, (iii) lower alkenyl, (v) lower alkoxy, (v) carboxy, (vi) lower alkoxy carbonyl, (vii) acyl, (viii) acyloxy, (ix) imino, (x) mercapto, (xi) lower alkylthio, (xii) carbamoyl, (xiii) lower alkylcarbamoyl, (xiv) cycloalkylcarbamoyl, (xv) thiocarbamoyl, (xvi) lower alkylthiocarbamoyl, (xvii) lower alkylsulfinyl, (xviii) lower alkylsulfonyl, (xix) sulfamoyl, (xx) lower alkylsulfamoyl and (xxi) cycloalkylsulfamoyl;

(7) the following groups (i) to (v), which are optionally substituted with the substituents group β, lower alkyl, lower alkoxy(lower)alkyl, optionally protected hydroxy(lower)alkyl, halogeno(lower)alkyl, lower alkylsulfonyl and/or arylsulfonyl,

(i) cycloalkyl, (ii) cycloalkenyl, (iii) cycloalkyloxy, (iv) amino and (v) alkylene dioxy; and

(8) the following groups (i) to (xii), which are optionally substituted with the substituents group β, lower alkyl, halo-

geno(lower)alkyl and/or oxo,

(i) phenyl, (ii) naphthyl, (iii) phenoxy, (iv) phenyl(lower)

alkoxy, (v) phenylthio, (vi) phenyl(lower)alkylthio, (vii) phenylazo, (viii) heterocycl, (ix) heterocyclxy, (x) hetero-

cyclthio, (xi) heterocyclcarbonyl and (xii) heterocyclsulfonyl.

The preferable examples of the substituents group α as substituents for Ring B are halogen; nitro; hydroxy; optionally substituted lower alkyl wherein the substituent(s) is halogen, cyano, phenyl, carboxy and/or lower alkoxy carbonyl;

lower alkenyl; lower alkoxy carbonyl(lower)alkenyl;

optionally substituted lower alkoxy wherein the substituent(s) is halogen, hydroxy, lower alkoxy, carboxy, lower alkoxy carbonyl, lower alkylamino and/or cyano; acyl; hydroxyimino; lower alkylthio; lower alkylsulfinyl; sulfamoyl;

optionally substituted amino wherein the substituent(s) is lower alkyl, optionally protected hydroxy(lower)alkyl, phenyl and/or acyl;

alkylene dioxy; cyanophenyl; heterocyclphenyl; biphenyl; phenoxy; phenylazo optionally substituted with lower alkyl; or

optionally substituted heterocycl wherein the substituent(s) is optionally protected hydroxy, mercapto, halogen, lower alkyl, cycloalkyl, lower alkoxy carbonyl, amino, lower alkoxy carbonyl amino, carbamoyl, oxo, phenyl, lower alkoxyphenyl or heterocycl. More preferable examples are halogen; lower alkyl optionally substituted with halogen; or lower alkoxy optionally substituted with halogen.

"A substituents group β" is a group consisting of halogen, optionally protected hydroxy, mercapto, lower alkoxy, lower alkenyl, amino, lower alkylamino, lower alkoxy carbonyl amino, lower alkylthio, acyl, carboxy, lower alkoxy carbonyl, carbamoyl, cyano, cycloalkyl, phenyl, phenoxy, lower alkylphenyl, lower alkoxyphenyl, halogenophenyl, naphthyl and heterocycl.

Examples of the substituents for "optionally substituted lower alkyl" represented by any other than Z (e.g., R¹) are one or more substituents selected from the substituents group β. The lower alkyl may be substituted with these substituents at any possible positions.

The lower alkyl part in "lower alkoxy", "lower alkoxy carbonyl", "lower alkoxy carbonyl(lower)alkyl", "lower alkylphenyl", "lower alkoxyphenyl", "lower alkylcarbamoyl", "lower alkylthiocarbamoyl", "lower alkylamino", "halogeno(lower)alkyl", "hydroxy(lower)alkyl", "phenyl(lower)alkoxy", "lower alkylthio", "phenyl(lower)alkylthio", "lower alkoxy carbonyl amino", "lower alkoxy carbonyl(lower)alkenyl", "lower alkylsulfinyl", "lower alkylsulfonyl", "aryl(lower)alkoxy carbonyl", "lower alkylbenzoyl" and "lower alkoxybenzoyl" is the same as defined in the above "lower alkyl".

Examples of the substituent(s) for "optionally substituted lower alkoxy" are one or more substituents selected from the substituents group β. Preferable examples are phenyl, lower alkylphenyl, lower alkoxyphenyl, naphthyl and heterocycl.

11

The term "cycloalkyl" includes C3 to C8 and preferably C5 to C6 cyclic alkyl. Examples are cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and cyclooctyl.

Examples of the substituent(s) for "optionally substituted cycloalkyl" are one or more substituents selected from the substituents group α and the cycloalkyl may be substituted with these substituents at any possible positions.

The term "bicycloalkyl" includes a group which is formed by excluding one hydrogen atom from a C5 to C8 aliphatic cycle containing two rings which possess two or more of atoms in common. Examples are bicyclo[2.1.0]pentyl, bicyclo[2.2.1]heptyl, bicyclo[2.2.2]octyl and bicyclo[3.2.1]octyl.

The term "lower alkenyl" includes C2 to C10, preferably C2 to C8 and more preferably C3 to C6 straight or branched alkenyl having one or more double bonds at any possible positions. Examples are vinyl, propenyl, isopropenyl, butenyl, isobut enyl, prenyl, butadienyl, pentenyl, isopentenyl, pentadienyl, hexenyl, isohexenyl, hexadienyl, heptenyl, octenyl, nonenyl and decenyl.

The "lower alkenyl" part in "lower alkoxy carbonyl(lower alkenyl)" is the same as the above "lower alkenyl".

Examples of the substituent(s) for "optionally substituted lower alkenyl" are halogen, lower alkoxy, lower alkenyl, amino, lower alkylamino, lower alkoxy carbonylamino, lower alkylthio, acyl, carboxy, lower alkoxy carbonyl, carbamoyl, cyano, cycloalkyl, phenyl, lower alkylphenyl, lower alkoxyphenyl, naphthyl and/or heterocyclyl.

The term "acyl" includes (1) C1 to C10, preferably C1 to C6 and more preferably C1 to C4 straight or branched alkylcarbonyl or alkenylcarbonyl, (2) C4 to C9 and preferably C4 to C7 cycloalkylcarbonyl and (3) C7 to C11 arylcarbonyl. Examples are formyl, acetyl, propionyl, butyryl, isobutyryl, valeryl, pivaloyl, hexanoyl, acryloyl, propioloyle, methacryloyl, crotonoyl, cyclopropylcarbonyl, cyclohexylcarbonyl, cyclooctylcarbonyl and benzoyl.

The "acyl" part in "acyloxy" is the same as the above.

The term "cycloalkenyl" includes a group having at least one double bond at any possible positions in the above cycloalkyl. Examples are cyclopropenyl, cyclobut enyl, cyclopentenyl, cyclohexenyl and cyclohexadienyl.

Examples of substituents for "optionally substituted cycloalkenyl" are one or more substituents selected from the substituents group β .

Examples of the substituent(s) for "optionally substituted amino" are the substituents group β , optionally substituted benzoyl and/or optionally substituted heterocyclylcarbonyl wherein the substituents is hydroxy, lower alkyl, lower alkoxy and/or lower alkylthio.

The term "aryl" includes a monocyclic or polycyclic aromatic carbocyclyl group and examples are phenyl, naphthyl, anthryl and phenanthryl. "Aryl" includes aryl fused with other a non-aromatic carbocyclyl group, for example, indanyl, indenyl, biphenyl, acenaphthyl, tetrahydronaphthyl and fluorenyl. Phenyl is preferable.

The aryl part in "aryl (lower) alkoxy carbonyl" is the same as the above.

The term "optionally substituted aryl" and "optionally substituted phenyl" represented by Z include the above "aryl" and "phenyl" respectively, which may be substituted with the substituents group α or lower alkyl which may be substituted with one or more group selected from the substituents group α .

Examples of the substituent(s) for "optionally substituted aryl" and "optionally substituted phenyl" represented by any other than Z are one or more groups selected from the substituents group β .

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The term "carbocyclyl" includes the above "cycloalkyl", "cycloalkenyl", "bicycloalkyl" and "aryl".

The term "non-aromatic carbocyclyl" includes the above "cycloalkyl", "cycloalkenyl" and "bicycloalkyl".

The term "optionally substituted carbocyclyl" includes the above "optionally substituted cycloalkyl", "optionally substituted cycloalkenyl", "optionally substituted bicycloalkyl" and "optionally substituted aryl".

The term "heterocyclyl" includes a heterocyclic group containing at least one heteroatom arbitrarily selected from O, S and N. For example, 5- or 6-membered heteroaryl such as pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazolyl, triazinyl, tetrazolyl, isoxazolyl, oxazolyl, oxadiazolyl, isothiazolyl, thiazolyl, thiadiazolyl, furyl and thienyl; fused heterocyclyl consisting of two rings such as indolyl, isoindolyl, indazolyl, indolizinyl, indolinyl, isoindolinyl, quinolyl, isoquinolyl, cinnolinyl, phthalazinyl, quinazolinyl, naphthyridinyl, quinoxalinyl, purinyl, pteridinyl, benzopyranyl, benzimidazolyl, benzisoxazolyl, benzoazolyl, benzoxadiazolyl, benzisothiazolyl, benzothiazolyl, benzothiadiazolyl, benzofuryl, isobenzofuryl, benzothienyl, benzotriazolyl, imidazopyridyl, triazoropyridyl, imidazothiazolyl, pyrazinopyridazinyl, tetrahydroquinolyl, tetrahydrobenzothienyl, oxazolopyridyl, thiadolo[5,4-b]pyridin-2-yl, thiadolo[5,4-c]pyridin-2-yl, thiadolo[4,5-b]pyridin-2-yl and thiadolo[4,5-c]pyridin-2-yl), benzoxazolinonyl, benzisoxazolinonyl, benzoxazinonyl, benzoxyazepinonyl, oxazolopyridinonyl and benzodioxolonyl; fused heterocyclyl consisting of three rings such as carbazolyl, acridinyl, xanthenyl, phenothiazinyl, phenoxathiinyl, phenoxazinyl and dibenzofuryl; and non-aromatic heterocyclyl such as dioxanyl, thiranyl, oxiranyl, oxathiolanyl, azetidinyl, thianyl, pyrrolidinyl, pyrrolinyl, imidazolidinyl, imidazolinyl, pyrazolidinyl, pyrazolinyl, piperidyl, piperazinyl, morpholinyl, morpholino, thiomorpholinyl, thiomorpholino, dihydropyridyl, tetrahydrofuryl, tetrahydropyranyl, tetrahydrothiazolyl and tetrahydroisothiazolyl.

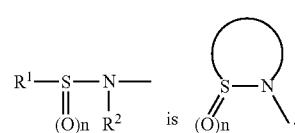
"Fused heterocyclyl" fused with a ring other than a heterocycle (e.g., benzothiazolyl), may connect at any possible position.

The substituent(s) for "optionally substituted heterocyclyl" and "optionally substituted fused heterocyclyl consisting of two rings" are the same as those for the above "optionally substituted aryl".

Heterocyclyl parts in "heterocyclylcarbonyl", "heterocyclyoxy", "heterocyclithio" and "heterocyclyl substituted phenyl" are the same as the above "heterocyclyl".

The term "lower alkylene" includes a bivalent group comprising 1 to 6 of methylene, preferably 2 to 6 of methylene and more preferably 3 to 6 of methylene. For example, methylene, ethylene, trimethylene, tetramethylene, pentamethylene and hexamethylene are included. Tetramethylene is preferable.

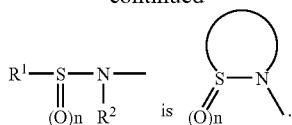
"R¹ and R² taken together may form lower alkylene" includes the case



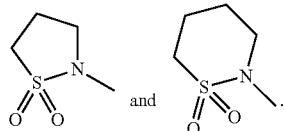
[Formula 31]

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Preferable examples are

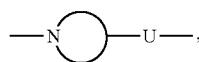


[Formula 32]

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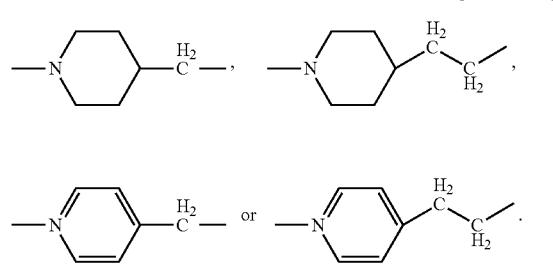
substituted phenylene”, “optionally substituted heterocyclyldiy” and “optionally substituted piperidinylene”. Halogen, hydroxy, lower alkyl, halogeno(lower)alkyl, lower alkoxy, amino, lower alkylamino, acyl, carboxy or lower alkoxy carbonyl is preferable. These substituents may attach to any possible positions.

When $-\text{NR}^2\text{X}-$ is a group of the formula:



[Formula 33]

U is preferably methylene or ethylene. More preferred is a group of the formula:



Lower alkylene part in “lower alkylene dioxy” is the same as the above “lower alkylene”. Methylene dioxy or ethylene dioxy is preferable.

The term “lower alkenylene” includes a bivalent group comprising 2 to 6 of methylene, preferably 3 to 6 of methylene and more preferably 4 to 5 of methylene and including at least one double bond.

The term “cycloalkylene” includes a bivalent group which is formed by excluding one hydrogen atom from the above “cycloalkyl”. A preferable example of cycloalkylene represented by X is 1,4-cyclohexanediyl.

The term “cycloalkenylene” includes a group containing at least one double bonds in the above cycloalkylene.

The term “bicycloalkylene” includes a group which is formed by excluding one hydrogen atom from the above “bicycloalkyl”. Examples are bicyclo[2.1.0]pentylene, bicyclo[2.2.1]heptylene, bicyclo[2.2.2]octylene and bicyclo[3.2.1]octylene.

The term “heterocyclyldiy” includes a bivalent group which is formed by excluding one hydrogen atom from the above “heterocyclyl”. Piperidinediy, piperazinediy, pyridinediy, pyrimidinediy, pyrazinediy, pyrrolidinediy or pyrrolediy is preferable. Piperidinediy is more preferable.

The term “arylene” includes a bivalent group which is formed by excluding one hydrogen atom from the above “aryl”. Phenylene is preferable.

The term “heteroarylene” includes aromatic groups in the above “heterocyclyldiy”. Examples are pyrrolediy, imidazolediy, pyrazolediy, pyridinediy, pyridazinediy, pyrimidinediy, pyrazinediy, triazolediy, triazinediy, isoazolediy, oxazolediy, oxadiaolediy, isothiazolediy, thiazolediy, thiadiaolediy, furandiy and thiophenediy.

One or more groups selected from the substituents group β are examples of substituents for “optionally substituted lower alkylene”, “optionally substituted lower alkenylene”, “optionally substituted cycloalkylene”, “optionally substituted cyclohexylene”, “optionally substituted bicycloalkylene”, “optionally substituted cycloalkenylene”, “optionally

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The compounds of the present invention include any formable and pharmaceutically acceptable salts thereof. Examples of “the pharmaceutically acceptable salt” are salts with mineral acids such as hydrochloric acid, sulfuric acid, nitric acid and phosphoric acid; salts with organic acids such as paratoluenesulfonic acid, methanesulfonic acid, oxalic acid and citric acid; salts with organic bases such as ammonium, trimethylammonium and triethylammonium; salts with alkaline metals such as sodium and potassium; and salts with alkaline earth metals such as calcium and magnesium.

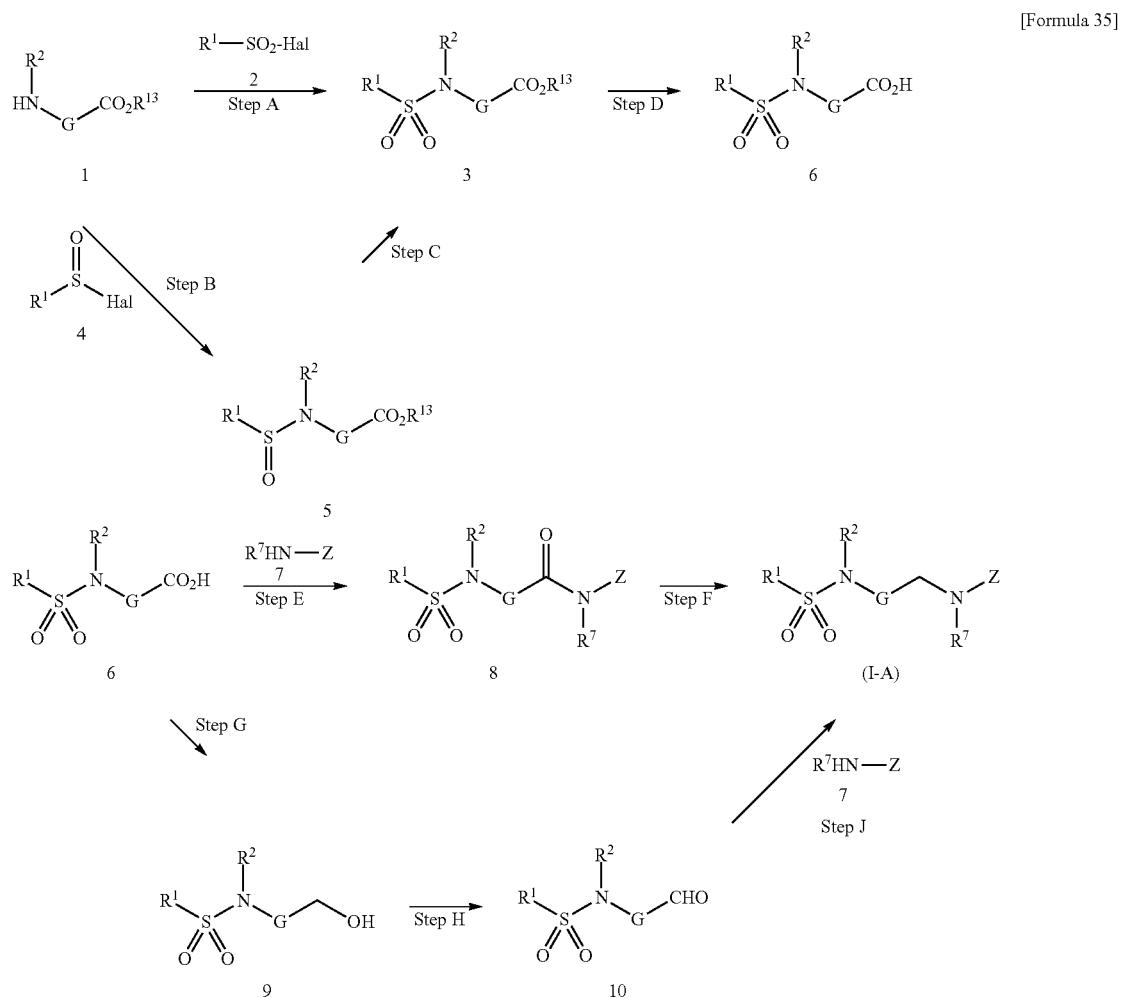
The compounds of the present invention include solvates thereof. Hydrate is preferable and arbitrary numbers of water molecules may coordinate to the compound of the present invention.

When Compound (I) of the present invention has an asymmetric carbon atom, it includes racemates, all of enantiomers and all of stereoisomers such as diastereomer, epimer and enantiomer thereof. When Compound (I) of the present invention having one or more double bonds forms an E isomer or Z isomer, Compound (I) includes both isomers. When X is cycloalkylene, Compound (I) includes both of cis isomer and trans isomer.

For example, Compound (I) of the present invention can be synthesized by the following methods. Hereinafter, X will be described as $-\text{CH}_2\text{-G-}$ or $-\text{G-CH}_2-$.

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[Compounds wherein Y=S(O)_n]

wherein Hal is halogen, -G-CH₂— is the same as —X— in the formula (I), R¹³ is lower alkyl and the other symbols are the same as the above.

Step A

Compound 1 is reacted with Sulfonyl Halide 2 having the desired substituent R¹ in a suitable solvent at 0° C. to 50° C. for several minutes to several hours to give Compound 3 wherein n is 2. Examples of the solvent are tetrahydrofuran, dimethylformamide, diethyl ether, dichloromethane, toluene, benzene, xylene, cyclohexane, hexane, chloroform, ethyl acetate, butyl acetate, pentane, heptane, dioxane, acetone, acetonitrile, water and a mixture thereof.

Step B

Compound 5 wherein n is 1 can be synthesized by reacting Compound 1 and Sulfinyl Halide 4 having substituent R¹. The conditions for the reaction are the same as those of the above Step A.

Step C

Compound 5 obtained in Step B is oxidized by the usual method to give Compound 3 wherein n is 2. Examples of an oxidizer are m-Chloroperbenzoic acid, peracetic acid, hydrogen peroxide, trifluoroperacetic acid, sodium periodate, sodium hypochlorite and potassium permanganate. The reaction may be carried out at 0° C. to 50° C. Examples of solvents

are tetrahydrofuran, dimethylformamide, diethyl ether, dichloromethane, toluene, benzene, xylene, cyclohexane, hexane, chloroform, ethyl acetate, butyl acetate, pentane, heptane, dioxane, acetone, acetonitrile, water, methanol, ethanol, isopropanol and mixture thereof.

Step D

Compound 3 obtained from Step A or C is treated in a suitable solvent and base to give Compound 6. Examples of the base are barium hydroxide, sodium hydroxide, potassium hydroxide, hydrazine, lithium salt of propanethiol. Examples of the solvent are tetrahydrofuran, dimethylformamide, dioxane, acetone, acetonitrile, methanol, ethanol, propanol, water and a mixed solvent thereof. The reaction may be carried out at 0° C. to 100° C. for several minutes to tens of hours.

Step E

Compound 6 obtained from Step D is reacted with Amino Compound 7 having the desired substituent Z and R⁷ in a suitable solvent at 0° C. to 50° C. for several minutes to several hours to give Compound 8. Examples of the solvent are tetrahydrofuran, dimethylformamide, diethyl ether, dichloromethane, toluene, benzene, xylene, cyclohexane, hexane, chloroform, ethyl acetate, butyl acetate, pentane, heptane, dioxane, acetone, acetonitrile, water and a mixed

solvent.

Compound 8 then reacts with R⁷HN-Z (Step F) to form Compound (I-A).

Compound (I-A) then reacts with water (Step G) to form Compound 9 (R1-S(=O)(=O)-N(R2)-G-CH₂-CH₂-OH).

17

solvent thereof. An activator such as thionyl chloride, acid halide, acid anhydride and activated ester can be used, if necessary.

Step F

The obtained Compound 8 is treated in a suitable solvent with a suitable reducing agent to give Compound (I-A). Examples of the reducing agent are sodium borohydride, lithium boron hydride and lithium aluminum hydride. Examples of the solvent are tetrahydrofuran, dimethylformamide, dioxane, acetonitrile, methanol, ethanol, propanol, acetic acid and a mixed solvent thereof. The reaction may be carried out at 0° C. to 100° C. for several minutes to tens of hours.

Step G

Compound 6 obtained from Step D is treated in a suitable solvent with a reducing agent to give Compound 9. Examples of reducing agent are sodium borohydride, lithium boron hydride, lithium aluminum hydride and diborane. Examples of the solvent are tetrahydrofuran, dimethylformamide, dioxane, acetonitrile, methanol, ethanol, propanol and a mixed solvent thereof. The reaction may be carried out at 0° C. to 100° C. for several minutes to tens of hours. Compound 9 can be obtained through the intermediate such as acid halide, acid anhydride and activated ester, if necessary.

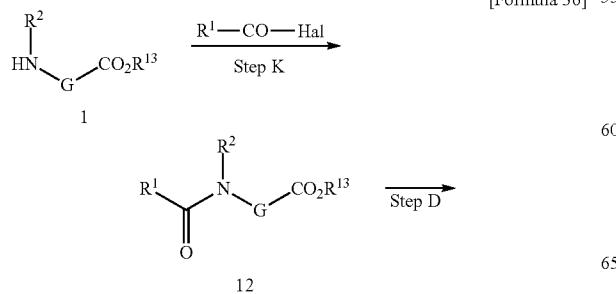
Step H

Compound 9 obtained from Step G is oxidized by the usual method to give Compound 10. Examples of an oxidizer are m-Chloroperbenzoic acid, peracetic acid, hydrogen peroxide, p-trifluoroacetic acid, sodium periodate, sodium hypochlorite, potassium permanganate, Dess-Martin periodinane, dimethylsulfoxide/oxalyl chloride (Swern oxidation) and ruthenium-catalyst. The reaction may be carried out at -80° C. to 50° C. Examples of the solvent are tetrahydrofuran, dimethylformamide, diethyl ether, dichloromethane, toluene, benzene, xylene, cyclohexane, hexane, chloroform, ethyl acetate, butyl acetate, pentane, heptane, dioxane, acetone, acetonitrile, water, methanol, ethanol, isopropanol and a mixed solvent thereof.

Step J

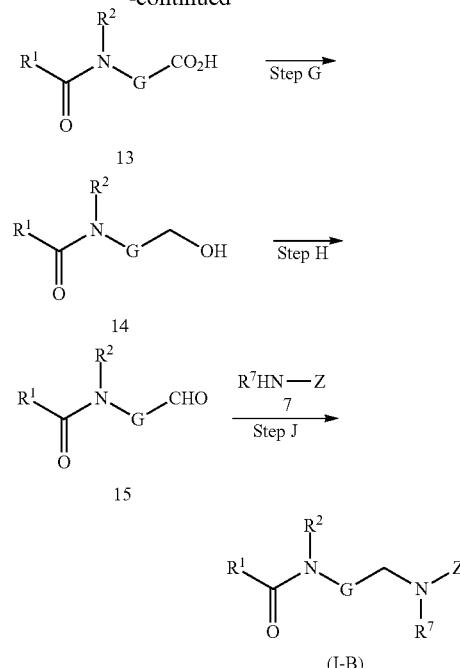
The obtained Compound 10 and Amino Compound 7 having the desired substituent Z and R⁷ are subjected to reductive amination reaction by a ordinary method to give Compound (I-A). Examples of the reducing agent are sodium borohydride, triacetoxy sodium borohydride and cyano sodium borohydride. The reaction may be carried out at 0° C. to 50° C. Examples of the solvent are tetrahydrofuran, dimethylformamide, dioxane, acetonitrile, methanol, ethanol, propanol, acetic acid, hydrochloric acid and a mixed solvent thereof.

[Compounds wherein Y=CO]



18

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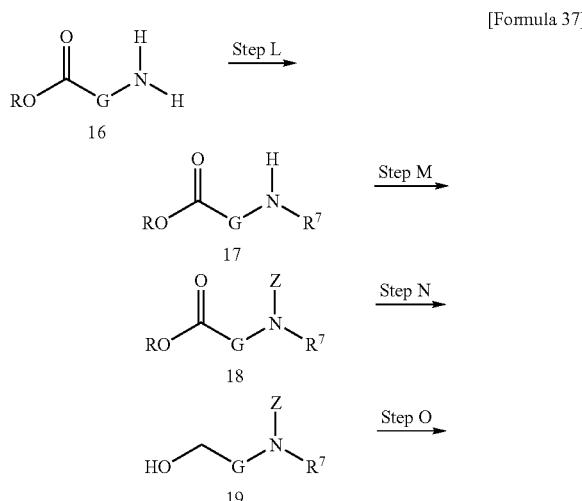
wherein each of the symbols is the same as the above and
³⁰ -G-CH₂- is the same as —X— in the formula (I).

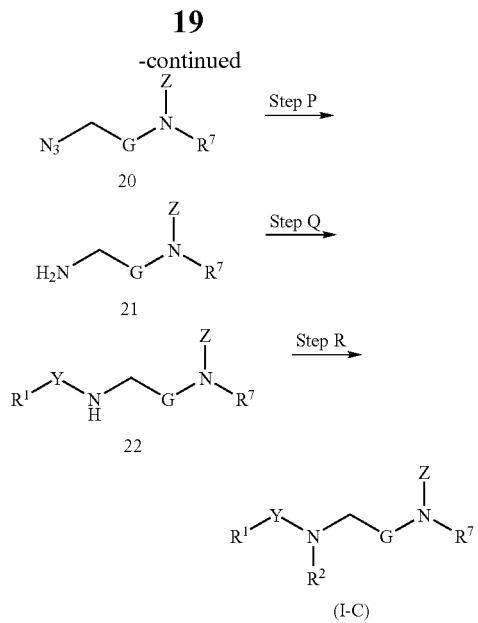
Step K

Compound 1 is reacted with Acyl Halide 11 having the desired substituent R¹ in a suitable solvent at -20° C. to 50° C. for several minutes to several hours to give Compound 12. Examples of the solvent are tetrahydrofuran, dimethylformamide, diethyl ether, dichloromethane, toluene, benzene, xylene, cyclohexane, hexane, chloroform, ethyl acetate, butyl acetate, pentane, heptane, dioxane, acetone, acetonitrile, water and a mixed solvent thereof.

Step D, G, H and J

The obtained Compound 12 is subjected to the similar method to the above Step D, G, H and J to give Compound 45 (I-B) of the present invention.





wherein each of the symbols is the same as the above, —CH₂—
G- is the same as —X— in the formula (I) and R is alkyl.

Step L

This is the step to introduce substituent R⁷ into Compound 16. For example, Compound 16 is reacted with R⁷X¹ wherein X¹ is halogen under the presence of a base to give Compound 17. Examples of the solvent are tetrahydrofuran and dimethylformamide. The reaction may be carried out at a room temperature. Examples of the base are triethylamine, pyridin and dimethylamino pyridin. The compound wherein R⁷ is hydrogen in formula (I-C) do not need this step.

Step M

This is the step to introduce substituent Z into Compound 17. For example, Compound 17 is reacted with ZX¹ wherein X¹ is halogen under the presence of a base to give Compound 18. Examples of the solvent are methanol, ethanol, isopropanol and dimethylformamide. The reaction may be carried out at a room temperature or under heating. For example, it can be carried out in a sealed tube by a microwave reactor. An example of the base is N,N-diisopropyl ethyl amine.

Step N

This is the step to reduce Compound 18 to give Compound 19. An example of reducing agent is lithium aluminum hydride. An example of the solvent is tetrahydrofuran. The reaction may be carried out at a room temperature.

Step O

This is the step to give Compound 20 by azidation of Compound 19. For example, methanesulfonyl chloride is reacted with Compound 19 by using triethylamine as a base to give mesylate. Chloroform can be used as the solvent for the mesylation. Sodium azide is reacted with the obtained compound and azidation is carried out in dimethylformamide or the like at room temperature or under warming to give Compound 20.

Step P

This is the step to reduce Compound 20 to give Compound 21. It can be carried out by catalytic reduction. An example of the catalyst is 10% palladium carbon. An example of the solvent is ethanol.

Step Q

This is the step to a compound of the formula: R¹—Y—X¹ wherein X¹ is halogen or the like, and Y is S, SO, SO₂ or CO is reacted with Compound 21 to give Compound 22.

20

Examples of a compound of the formula: R¹—Y—X¹ are various sulfonyl chloride and acyl chloride. Examples of the solvent are tetrahydrofuran and dimethylamide. The reaction may be carried out at a room temperature or under heating.

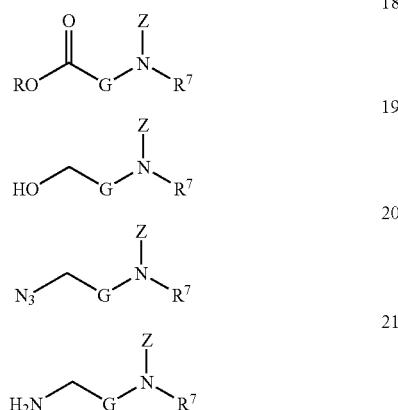
The reaction is preferably carried out under a base. Examples of the base are pyridin and triethylamine. A compound wherein R² is hydrogen in the formula (I-C) do not need the subsequent Step R and Compound 22 is a final target compound. This reaction can be carried out with a compound of the formula: R¹—Y—X¹ wherein Y=S or SO to give Compound 22, and then the oxidation can be carried out to transform to a compound wherein Y is SO₂ used for the next step.

Step R

This is the step to introduce substituent R² into Compound 22. R²X¹ wherein X¹ is halogen or the like is reacted with Compound 22 under the presence of a base to give Compound (I-C). An example of base is sodium hydride. An example of the solvent is dimethylformamide.

The following intermediates are useful in the above steps.

[Formula 38]



wherein

R is optionally substituted lower alkyl,
R7 is hydrogen or optionally substituted lower alkyl,
G is 1,4-cycloalkylene, and
Z is optionally substituted carbocyclyl or optionally substituted heterocyclyl.

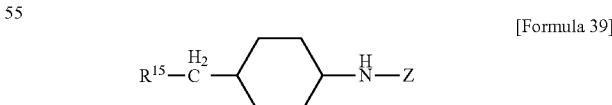
R is preferably lower alkyl and more preferably methyl and ethyl. Ethyl is especially preferable.

Preferable R7 is hydrogen.

Preferable Z is optionally substituted heterocyclyl.

The following compounds are especially preferable.

A compound of the formula:

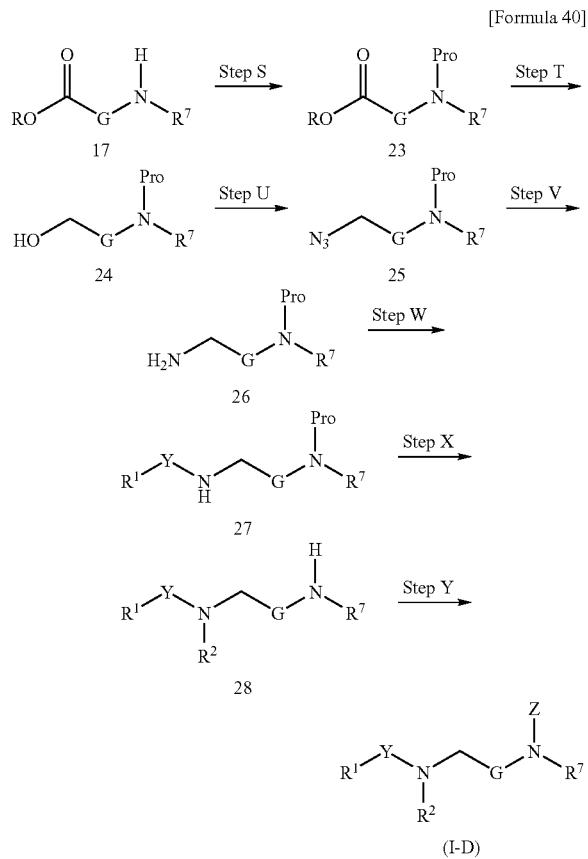


wherein

R15 is NH₂ or OH, and

Z is optionally substituted pyridyl, optionally substituted pyridazinyl, optionally substituted pyrazinyl, optionally substituted pyrimidinyl, optionally substituted quinolyl, optionally substituted isoquinolyl, optionally substituted benzothiiazolyl, optionally substituted benzoxazolyl, optionally

substituted benzopyridyl, optionally substituted benzopyridazinyl, optionally substituted benzimidazolyl, optionally substituted benzoxazolyl, optionally substituted thiazolopyridyl optionally substituted benzisoxazolinonyl, optionally substituted benzoxazolinonyl, optionally substituted benzoxazinonyl or optionally substituted benzoxyazepinonyl.



wherein each of the symbols is the same as the above, —CH₂—G— is the same as —X— in the formula (I), R is alkyl and Pro is amino protecting group.

Step S

This is the step to introduce a protecting group into Compound 17. As a protecting group, the protecting group described in Protective Groups in Organic Synthesis (Theodora W. Greene) or the like can be used. The amino protecting groups which can be removed under the acid condition are preferable. Examples are benzyloxycarbonyl and tert-butyloxycarbonyl. For example, ProX¹ wherein X¹ is halogen or the like and Pro is benzyloxycarbonyl, tert-butyloxycarbonyl or the like and Pro-O-Pro wherein Pro is benzyloxycarbonyl, tert-butyloxycarbonyl or the like are reacted under the presence of the base to give Compound 23. Examples of the solvent are tetrahydrofuran and dimethylformamide. The reaction may be carried out at a room temperature. Examples of the base are triethylamine, pyridine and dimethyl amino pyridine. The reaction also can be carried out with a compound wherein R⁷ is hydrogen.

Step T

This is the step to reduce Compound 23 to give Compound 24. Lithium aluminum hydride can be used as the reducing agent. An example of the solvent is tetrahydrofuran. The reaction may be carried out at a room temperature.

Step U

This is the step to give Compound 25 by azidation of Compound 24. For example, methanesulfonyl chloride is reacted with Compound 24 by using triethylamine as a base to give mesylate. Chloroform can be used as the solvent for the mesylation. Sodium azide is reacted with the obtained compound and azidation is carried out in dimethylformamide or the like at room temperature or under warming to give Compound 25.

Step V

This is the step to reduce Compound 25 to give Compound 26. Compound 25 is reduced with triphenylphosphine and water to give Compound 26. The reaction may be carried out under heating. An example of the solvent is tetrahydrofuran. Except for the reduction method with triphenylphosphine, the catalytic reduction can be used. For the catalytic reduction, 10% palladium carbon or the like can be used as catalyst. An example of the solvent is ethanol. The reduction method can be suitably selected depending on the used protecting group.

Step W

This is the step to react a compound of the formula: R¹—Y—X¹ wherein X¹ is halogen or the like, Y is S, SO, SO₂ or CO with Compound 26 to give Compound 27. Examples of the compound of the formula: R¹—Y—X¹ wherein X¹ is halogen or the like are various sulfonyl chloride and acyl chloride. Examples of the solvent are tetrahydrofuran and dimethylamide. The reaction may carry out at a room temperature or under heating. The reaction is preferably carried out under a base. Examples of the base are pyridine and triethylamine. This reaction can be carried out with a compound of the formula: R¹—Y—X¹ wherein Y=S or SO to give Compound 27, and then the oxidation can be carried out to transform to a compound wherein Y is SO₂ used for the next step.

Step X

This is the step to remove the protecting group of Compound 27. The method for removing the protecting group can be used by selecting various conditions depending on the protecting group. For example, tert-butyloxycarbonyl can be removed with acid. Benzyloxycarbonyl can be removed by catalytic reduction or the like.

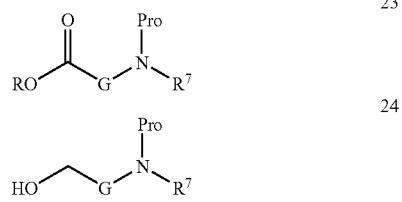
Step Y

This is the step to introduce substituent Z into Compound 28. For example, ZX¹ wherein X¹ is halogen is reacted under the presence of the base to give Compound (I-D). Examples of the solvent are methanol, ethanol, isopropanol and dimethylformamide. The reaction may carry out at a room temperature or under heating. For example, it can be carried out in a sealed tube by a microwave reactor. An example of the base is N,N-diisopropyl ethyl amine.

In the above steps, the following intermediates are useful.

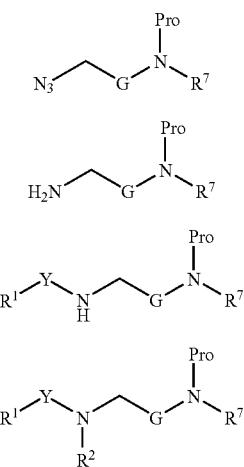
A compound of the formula:

[Formula 41]



23

-continued

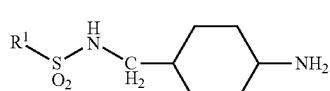


wherein

 R is optionally substituted lower alkyl, Pro is a protecting group, R^7 is hydrogen or optionally substituted lower alkyl, G is 1,4-cycloalkylene, Y is SO_2 or SO , R' is optionally substituted lower alkyl, and R^2 is hydrogen or optionally substituted lower alkyl. R is preferably lower alkyl and more preferably methyl and ethyl. Ethyl is especially preferable.Preferable Pro is amino protecting group which can be removed under the acid condition. Examples of Pro are the formula: $-(\text{C}=\text{O})-\text{O}-\text{R}^X$, wherein R is optionally substituted lower alkyl, optionally substituted lower alkenyl. Tert-butyloxycarbonyl is especially preferable.Preferable R^7 is hydrogen.Preferable Y is SO_2 . R' is preferably lower alkyl and more preferably isopropyl and ethyl. Ethyl is especially preferable.Preferable R^2 is hydrogen.

The following compounds are especially preferable.

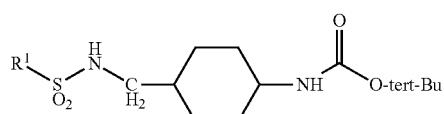
A compound of the formula:



[Formula 42]

wherein R^1 is ethyl or tert-butyl.

A compound of the formula:

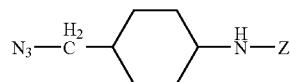


[Formula 43]

wherein R^1 is ethyl, isopropyl or tert-butyl.

24

A compound of the formula:



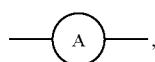
[Formula 44]

wherein Z is optionally substituted carbocyclol or optionally substituted heterocyclol.

All of the compounds of the present invention have an NPY Y5 antagonistic activity and the following compounds are especially preferable.

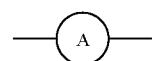
In the formula (I),

- 28 15 a compound wherein R^1 is optionally substituted lower alkyl (hereinafter referred to as “ R^1 is R1-1”),
 a compound wherein R^1 is C1 to C10 alkyl optionally substituted with halogen (hereinafter referred to as “ R^1 is R1-2”),
 a compound wherein R^1 is C1 to C10 alkyl optionally substituted with halogen (hereinafter referred to as “ R^1 is R1-3”),
 20 a compound wherein R^1 is isopropyl or t-butyl (hereinafter referred to as “ R^1 is R1-4”),
 a compound wherein R^2 is hydrogen or C1 to C3 alkyl (hereinafter referred to as “ R^2 is R2-1”),
 25 a compound wherein R^2 is hydrogen (hereinafter referred to as “ R^2 is R2-2”),
 a compound wherein X is optionally substituted lower alkylene, optionally substituted lower alkenylene or a group of the formula:



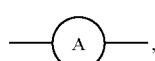
[Formula 45]

wherein a group of the formula:



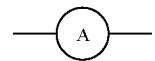
[Formula 46]

- 35 is optionally substituted cycloalkylene, optionally substituted cycloalkenylene, optionally substituted bicycloalkylene, optionally substituted phenylene or optionally substituted heterocyclediyl (hereinafter referred to as “ X is X-1”),
 a compound wherein X is C2 to C6 alkylene, C3 to C6 alkenylene or a group of the formula:



[Formula 47]

55 wherein a group of the formula:



[Formula 48]

- 60 is optionally substituted cycloalkylene, optionally substituted cycloalkenylene, optionally substituted bicycloalkylene, optionally substituted phenylene, optionally substituted piperidinylene, optionally substituted thiophenediyl or optionally substituted furandiyl (hereinafter referred to as “ X is X-2”),

25

a compound wherein X is C2 to C6 alkylene or a group of the formula:



wherein a group of the formula:



wherein is optionally substituted cycloalkylene, optionally substituted phenylene, optionally substituted piperidinylene, optionally substituted thiophenediy or optionally substituted furandiy (hereinafter referred to as "X is X-3"),

a compound wherein X is (i) C2 to C6 alkylene or (ii) cycloalkylene or phenylene, each of which is optionally substituted with halogen, hydroxy, lower alkyl or halogeno(lower)alkyl (hereinafter referred to as "X is X-4"),

a compound wherein X is C2 to C6 alkylene or to C5 to C6 cycloalkylene (hereinafter referred to as "X is X-5"),

a compound wherein X is C3 to C6 alkylene or 1,4-cyclohexylene (hereinafter referred to as "X is X-6"),

a compound wherein Y is —SO— (hereinafter referred to as "Y is Y-1"),

a compound wherein Y is —SO₂— (hereinafter referred to as "Y is Y-2"),

a compound wherein Y is —CO— (hereinafter referred to as "Y is Y-3"),

a compound wherein Z is optionally substituted lower alkyl, optionally substituted carbocycl or optionally substituted heterocycl (hereinafter referred to as "Z is Z-1"),

a compound wherein Z is a group of the formula:—(CR⁸, R⁹)r—W—(CR¹⁰R¹¹)s—V

wherein

R⁸, R⁹, R¹⁰ and R¹¹ are each independently hydrogen or lower alkyl and when Z has two or more of R⁸, two or more of R⁹, two or more of R¹⁰ and/or two or more of R¹¹, each of R⁸, R⁹, R¹⁰ and R¹¹ may be different,

W is single bond, O, S or NR¹²,

R¹² is hydrogen, lower alkyl or phenyl,

V is hydrogen, optionally substituted cycloalkyl, optionally substituted bicycloalkyl, optionally substituted aryl or optionally substituted heterocycl,

r is an integer of 1 to 4 and

s is an integer of 0 to 4

(hereinafter referred to as "Z is Z-2"),

a compound wherein Z is a group of the formula:—(CH₂)r—W—(CH₂)s—V

wherein

W is single bond, O, S or NR¹²,

R¹² is hydrogen or lower alkyl,

V is optionally substituted aryl or optionally substituted heterocycl

wherein the substituent(s) is halogen, hydroxy, lower alkyl, halogeno(lower)alkyl, lower alkoxy, lower alketyl, amino, lower alkylamino, acyl, carboxy, lower alkoxy carbonyl, phenyl or monocyclic heteroaryl,

[Formula 49]

5

26

r is an integer of 1 to 4 and
s is an integer of 0 to 4
(hereinafter referred to as "Z is Z-3"),
a compound wherein Z is a group of the formula:—(CH₂)r—W—(CH₂)s—V

wherein

W is single bond, O, S, NH or NMe,
V is optionally substituted phenyl or optionally substituted heteroaryl

wherein the substituents is halogen, lower alkyl, halogeno(lower)alkyl, lower alkoxy, amino or lower alkylamino,
r is an integer of 1 to 3 and
s is an integer of 0 or 1

(hereinafter referred to as "Z is Z-4"),
a compound wherein Z is optionally substituted carbocycl,
15 wherein the substituent is halogen; hydroxy;
optionally substituted lower alkyl wherein the substituent(s) is halogen, hydroxy, carboxy, lower alkoxy carbonyl, cyano and/or phenyl;
lower alketyl optionally substituted with lower alkoxy carbonyl;

20 optionally substituted lower alkoxy wherein the substituent(s) is halogen, hydroxy, lower alkoxy, carboxy, lower alkoxy carbonyl, lower alkylamino, cycloalkyl, cyano and/or heterocycl;

25 cycloalkyl; cycloalkyloxy; acyl; lower alkylthio; carbamoyl; lower alkylcarbamoyl; cycloalkylcarbamoyl; hydroxy imino;
optionally substituted amino wherein the substituent(s) is lower alkyl, optionally protected hydroxy(lower)alkyl, lower alkoxy(lower)alkyl, acyl, lower alkylsulfonyl, arylsulfonyl and/or phenyl;

30 phenyl optionally substituted with halogen, cyano, phenyl and/or heterocycl;
lower alkylsulfinyl; lower alkylsulfamoyl; cycloalkylsulfamoyl;

35 nitro; cyano; alkylenedioxy; phenylazo optionally substituted with lower alkyl; phenoxy; o xo;

optionally substituted heterocycl wherein the substituent(s) is optionally protected hydroxy, mercapto, halogen, lower alkyl, cycloalkyl, lower alkoxy carbonyl, acyl, amino, lower alkoxy carbonyl amine, carbamoyl, oxo, phenyl, lower alkoxyphenyl, halogenophenyl, heterocycl and/or o xo;

40 heterocyclsulfonyl optionally substituted with lower alkyl; heterocyclloxy; heterocyclcarbonyl optionally substituted with lower alkyl (hereinafter referred to as "Z is Z-5"),

a compound wherein Z is optionally substituted phenyl wherein the substituent(s) is halogen; hydroxy; lower alkyl optionally substituted with halogen, hydroxy, lower alkoxy carbonyl, cyano and/or phenyl; lower alkoxy carbonyl(lower)alkenyl; lower alkoxy optionally substituted with halogen,

lower alkoxy, lower alkoxy carbonyl, cycloalkyl and/or heterocycl; cycloalkyl; cycloalkyloxy; acyl; lower alkylthio; carbamoyl; lower alkylcarbamoyl; amino optionally substituted with lower alkyl, hydroxy(lower)alkyl, acyl, lower alkylsulfonyl and/or phenyl; phenyl optionally substituted with halogen, cyano, phenyl and/or heterocycl; lower alkyl sulfamoyl; cycloalkylsulfamoyl; nitro; alkylenedioxy; phenylazo optionally substituted with lower alkyl; phenoxy; o xo;

55 heterocycl optionally substituted with hydroxy, halogen, lower alkyl, lower alkoxy carbonyl, amino, carbamoyl, phenyl, halogenophenyl, heterocycl and/or o xo; heterocyclloxy; and/or heterocyclsulfonyl optionally substituted with lower alkyl (hereinafter referred to as "Z is Z-6"),

a compound wherein Z is optionally substituted phenyl wherein the substituent(s) is halogen; lower alkyl optionally substituted with halogen, hydroxy, lower alkoxy carbonyl and/or phenyl; lower alkoxy optionally substituted with halogen and/or cycloalkyl; cycloalkyl; cycloalkyloxy; acyl; lower alkylthio; lower alkylcarbamoyl; amino optionally substi-

60 tuted with halogen, hydroxy, lower alkoxy carbonyl, amino, carbamoyl, phenyl, halogenophenyl, heterocycl and/or o xo; heterocyclloxy; and/or heterocyclsulfonyl optionally substituted with lower alkyl (hereinafter referred to as "Z is Z-7"),

tuted with lower alkyl, hydroxy(lower)alkyl, acyl and/or phenyl; phenyl optionally substituted with piperidyl; cycloalkylsulfamoyl; alkyleneoxy; phenoxy; morpholinyl or morpholino, each of which is optionally substituted with lower alkyl; piperidyl optionally substituted with hydroxy, lower alkyl, lower alkoxy carbonyl, phenyl, halogenophenyl and/or oxo; pyrrolidinyl optionally substituted with hydroxy, carbamoyl and/or oxo; piperazinyl optionally substituted with phenyl or pyrimidinyl; dihydropyridyl; pyrrolyl; pyrrolinyl; imidazolyl optionally substituted with halogen and/or lower alkyl; pyrazolyl; thiényl; thiadiazolyl; furyl; oxazolyl; isoxazolyl; tetrazolyl optionally substituted with lower alkyl and/or phenyl; indolinyl; indolyl; tetrahydroquinolyl; benzothiazolyl optionally substituted with lower alkyl; tetrahydroisothiazolyl optionally substituted with oxo; benzopyranyl optionally substituted with oxo; tetrahydropyranloxy; tetrahydrofuryloxy; morpholinosulfonyl optionally substituted with lower alkyl; and/or piperidylsulfonyl optionally substituted with lower alkyl (hereinafter referred to as "Z is Z-7"), a compound wherein Z is optionally substituted phenyl wherein the substituent(s) is halogen, lower alkyl, halogeno(lower)alkyl, lower alkoxy, cycloalkyloxy, lower alkylcarbamoyl, phenyl, lower alkyl morpholino and/or tetrahydropyranloxy (hereinafter referred to as "Z is Z-8"), a compound wherein Z is optionally substituted heterocyclyl wherein the substituent(s) is halogen, hydroxy, lower alkyl, halogeno(lower)alkyl, lower alkoxy, mercapto, lower alkylthio, acyl, carboxy, lower alkoxy carbonyl, amino, lower alkylamino, phenyl, naphthyl, phenylthio optionally substituted with halogen, phenoxy optionally substituted with halogen, oxo, and/or heterocyclyl optionally substituted with lower alkyl (hereinafter referred to as "Z is Z-9"), a compound wherein Z is thienyl, pyrazolyl, thiazolyl, thiadiazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, indolyl, isoindolyl, indolinyl, isoindolinyl, indazolyl, benzopyranyl, benzoxazolyl, benzothienyl, benzothiazolyl, benzothiazolinyl, benzothiadiazolyl, benzimidazolyl, quinolyl, isoquinolyl, dihydrobenzofuryl, carbazolyl, acridinyl, dibenzofuryl or thiazolopyridyl, each of which is optionally substituted with substituents selected from the group of lower alkyl; halogeno(lower)alkyl; lower alkoxy; lower alkoxy carbonyl; acyl; lower alkoxy carbonyl(lower)alkyl; mercapto; phenyl, naphthyl, phenylthio or phenoxy, each of which is optionally substituted with halogen; furyl; nitro; oxo; and morpholino optionally substituted with lower alkyl (hereinafter referred to as "Z is Z-10"), a compound wherein Z is thienyl, thiazolyl, thiadiazolyl, pyridyl, pyrazinyl, indolyl, isoindolinyl, benzopyranyl, quinolyl, carbazolyl, dibenzofuryl, benzopyranyl, benzothienyl or benzothiazolyl, each of which is optionally substituted with one or more substituent(s) selected from the group of lower alkyl, halogeno(lower)alkyl, lower alkoxy, lower alkoxy carbonyl, acyl, phenyl, naphthyl, phenylthio, lower alkyl morpholino and oxo) (hereinafter referred to as "Z is Z-11"), a compound wherein R¹ is R¹⁻², R² is R²⁻², n is 2 and a combination of X, Y and Z, i.e., (X, Y, Z), is any one of the followings.

(X, Y, Z)=(X-3, Y-2, Z-1), (X-3, Y-2, Z-2), (X-3, Y-2, Z-3), (X-3, Y-2, Z-4), (X-3, Y-2, Z-5), (X-3, Y-2, Z-6), (X-3, Y-2, Z-7), (X-3, Y-2, Z-8), (X-3, Y-2, Z-9), (X-3, Y-2, Z-10), (X-3, Y-2, Z-11), (X-3, Y-3, Z-1), (X-3, Y-3, Z-2), (X-3, Y-3, Z-3), (X-3, Y-3, Z-4), (X-3, Y-3, Z-5), (X-3, Y-3, Z-6), (X-3, Y-3, Z-7), (X-3, Y-3, Z-8), (X-3, Y-3, Z-9), (X-3, Y-3, Z-10), (X-3, Y-3, Z-11), (X-4, Y-2, Z-

5), (X-4, Y-2, Z-6), (X-4, Y-2, Z-7), (X-4, Y-2, Z-8), (X-4, Y-2, Z-9), (X-4, Y-2, Z-10), (X-4, Y-2, Z-11), (X-4, Y-3, Z-1), (X-4, Y-3, Z-2), (X-4, Y-3, Z-3), (X-4, Y-3, Z-4), (X-4, Y-3, Z-5), (X-4, Y-3, Z-6), (X-4, Y-3, Z-7), (X-4, Y-3, Z-8), (X-4, Y-3, Z-9), (X-4, Y-3, Z-10), (X-4, Y-3, Z-11), (X-5, Y-2, Z-1), (X-5, Y-2, Z-2), (X-5, Y-2, Z-3), (X-5, Y-2, Z-4), (X-5, Y-2, Z-5), (X-5, Y-2, Z-6), (X-5, Y-2, Z-7), (X-5, Y-2, Z-8), (X-5, Y-2, Z-9), (X-5, Y-2, Z-10), (X-5, Y-2, Z-11), (X-5, Y-3, Z-1), (X-5, Y-3, Z-2), (X-5, Y-3, Z-3), (X-5, Y-3, Z-4), (X-5, Y-3, Z-5), (X-5, Y-3, Z-6), (X-5, Y-3, Z-7), (X-5, Y-3, Z-8), (X-5, Y-3, Z-9), (X-5, Y-3, Z-10) or (X-5, Y-3, Z-11) the pharmaceutically acceptable salt or solvate thereof.

The NPY Y5 receptor antagonist of the present invention is effective for all of the diseases in which NPY Y5 is involved and it is especially useful for preventing and/or treating obesity and suppressing food intake. Moreover, the antagonist is effective for preventing and/or treating the diseases in which obesity acts as a risk factor, for example, diabetes, hypertension, hyperlipemia, atherosclerosis and acute coronary syndrome.

Furthermore, a compound of the present invention has not only NPY Y5 receptor antagonistic activity but also any or all good characters as a medicine selected from the followings.

- 25 a) weak CYP enzyme inhibition
- b) less induction of a drug-metabolizing enzyme.
- c) good drug disposition such as high bioavailability.
- d) low toxicity of anemia-inducing activity or the like.
- e) high metabolic stability.
- f) high selectivity for Y5 receptor.
- 30 g) high water solubility.
- h) high transportability through the blood-brain barrier.

In addition, the NPY Y5 receptor antagonist of the present invention has a low affinity for NPY Y1 and Y2 receptors, and 35 has a high selectivity for NPY Y5 receptor. NPY causes a sustained vasoconstrictive action in the periphery and this action is mainly via Y1 receptor. Since Y5 receptor is not involved in this action at all, the NPY Y5 receptor antagonist has a low risk of inducing side effects based on the peripheral 40 vasoconstriction, and is expected to be suitably used as a safe medicine.

The NPY Y5 receptor antagonist shows an anti-obesity effect by suppressing food intake. Therefore, it is one of the features of the present antagonist not to induce side effects such as dyspepsia caused by an anti-obesity agent which inhibits digestion and absorption, or central nervous system side-effects such as an antidepressant effect due to a serotonin transporter inhibitor that shows an anti-obesity effect.

A compound of the present invention can be administered orally or parenterally as an anti-obesity agent or anorectic agent. In the case of oral administration, it may be in any usual form such as tablets, granules, powders, capsules, pills, solutions, syrups, buccal tablets and sublingual tablets. When the compound is parenterally administered, any usual form is preferable, for example, injections (e.g., intravenous, intramuscular), suppositories, endermic agents and inhalations. Oral administration is especially preferable because the compounds of the present invention show a high oral absorbability.

60 A pharmaceutical composition may be manufactured by mixing an effective amount of a compound of the present invention with various pharmaceutical additives suitable for the administration form, such as excipients, binders, moistening agents, disintegrants, lubricants and diluents. When the 65 composition is of an injection, an active ingredient together with a suitable carrier can be sterilized to give a pharmaceutical composition.

29

Examples of the excipients include lactose, saccharose, glucose, starch, calcium carbonate and crystalline cellulose. Examples of the binders include methylcellulose, carboxymethylcellulose, hydroxypropylcellulose, gelatin and polyvinylpyrrolidone. Examples of the disintegrants include carboxymethylcellulose, sodium carboxymethylcellulose, starch, sodium alginate, agar and sodium lauryl sulfate. Examples of the lubricants include talc, magnesium stearate and macrogol. Cacao oil, macrogol, methylcellulose or the like may be used as base materials of suppositories. When the composition is manufactured as solutions, emulsified injections or suspended injections, solubilizing agents, suspending agents, emulsifiers, stabilizers, preservatives, isotonic agents and the like which are usually used may be added. For oral administration, sweetening agents, flavors and the like which are usually used may be added.

Although the dosage of a compound of the present invention as an anti-obesity agent or anorectic agent should be determined in consideration of the patient's age and body weight, the type and degree of diseases, the administration route and the like, a usual oral dosage for an adult is 0.05 to 100 mg/kg/day and preferable is 0.1 to 10 mg/kg/day. For parenteral administration, although the dosage highly varies with administration routes, a usual dosage is 0.005 to 10 mg/kg/day and preferably 0.01 to 1 mg/kg/day. The dosage may be administered in one to several divisions per day.

The present invention is further explained by the following Examples, which are not intended to limit the scope of the present invention.

The abbreviations used in the present description stand for the following meanings.

Me: methyl

Et: ethyl

i-Pr: isopropyl

DMSO: dimethylsulfoxide

Pd—C: palladium carbon

THF: tetrahydrofuran

DMF: N,N-dimethylformamide

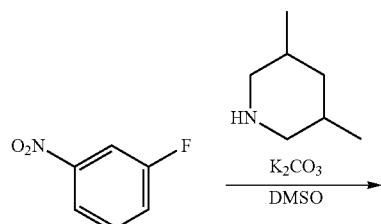
mCPBA: meta-Chloroperoxybenzoic acid

Example 1

Synthesis of Compound (Ii-1)

Step 1

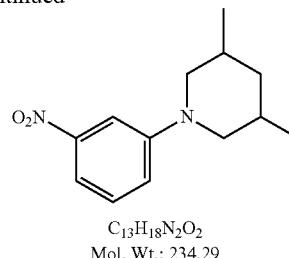
[Formula 51]



$C_6H_4FNO_2$
Mol. Wt.: 141.1

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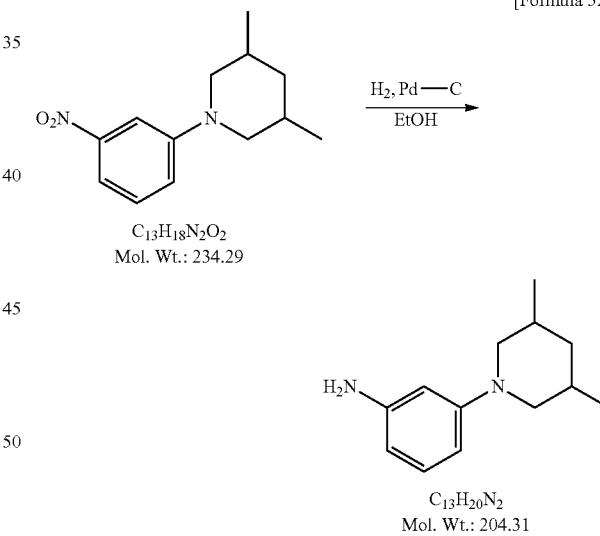


3-fluoronitrobenzene (2.00 g, 14.2 mmol) was dissolved in 15 dimethylsulfoxide (15 ml). 3,5-dimethylpiperidine (3.21 g, 28.4 mmol) and potassium carbonate (3.92 g, 28.4 mmol) were added thereto and the mixture was stirred for 3 hours at 150° C. The reactant was poured into water and extracted with ethyl acetate. The organic layer was washed with water and 20 dried over sodium sulphate anhydrous. The solvent was removed under reduced pressure. Ethyl acetate and hexane were added to the residue. The precipitated crystals were collected with filtration to give the desired substituted 25 nitrobenzene (2.05 g, 62% yield).

1H-NMR ($CDCl_3$) δ ppm: 0.76 (q, 1H, $J=12.0$ Hz), 0.96 (d, 6H, $J=6.3$ Hz), 1.70-1.91 (m, 3H), 2.32 (t, 2H, $J=12.0$ Hz), 30 3.62-3.72 (m, 2H), 7.17-7.25 (m, 1H), 7.34 (t, 1H, $J=8.1$ Hz), 7.59 (d, 1H, $J=8.1$ Hz), 7.71 (s, 1H).

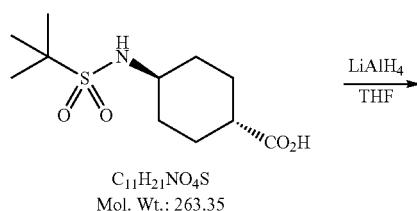
Step 2

[Formula 52]



The compound obtained in Step 1 (2.05 g, 8.75 mmol) was dissolved in ethanol (25 ml) and 10% Pd—C(0.20 g) was added thereto to carry the hydrogenation reaction for 12 hours. Pd—C was removed by celite filtration and the filtrate 60 was condensed under reduced pressure. The residue was purified by silica gel chromatography to give the desired aniline (1.62 g, 90% yield).

1H-NMR ($CDCl_3$) δ ppm: 0.69 (q, 1H, $J=12.0$ Hz), 0.92 (d, 6H, $J=6.3$ Hz), 1.75-1.98 (m, 3H), 2.22 (t, 2H, $J=12.0$ Hz), 3.53-3.62 (m, 2H), 6.21 (d, 1H, $J=7.5$ Hz), 6.38 (s, 1H), 6.42 (d, 1H, $J=8.1$ Hz), 7.04 (t, 1H, $J=8.1$ Hz).

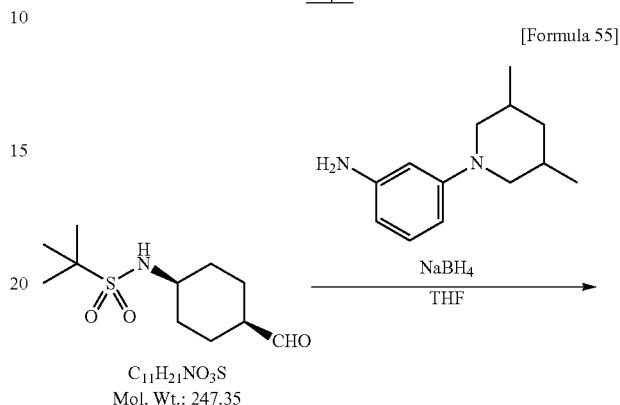
31Step 3

[Formula 53]

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removed by filtration, the filtrate was condensed under reduced pressure. The residue was purified by silica gel chromatography to give the desired aldehyde (385 mg, 77° A) yield.

1H-NMR (DMSO-d6) δ ppm: 1.26 (s, 9H), 1.13-1.38 (m, 4H), 1.85-1.98 (m, 4H), 2.16 (m, 1H), 3.01 (m, 1H), 6.80 (d, 1H, J =8.0 Hz), 9.54 (s, 1H).

Step 5

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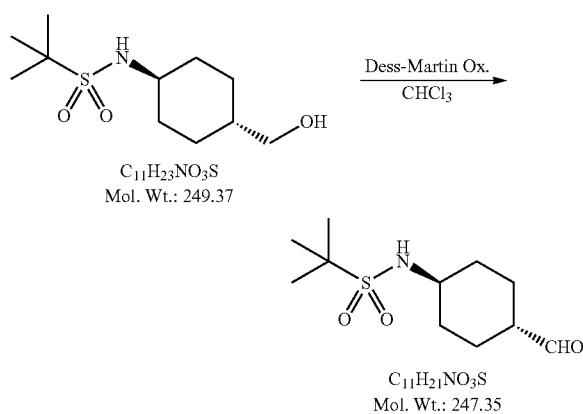
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Step 4

[Formula 54]



Aniline obtained in Step 2 (107 mg, 0.523 mmol) was dissolved in tetrahydrofuran (3 ml). Aldehyde obtained in Step 4 (130 mg, 0.523 mmol) was added thereto and the mixture was stirred at room temperature for 1 hour. To the reactant, was added sodium borohydride (23.7 mg, 0.628 mmol) and the mixture was stirred at room temperature for 3 hours. The reactant was poured into water and extracted with ethyl acetate. The organic layer was washed with water and dried over sodium sulphate anhydrous. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography to give the desired compound (99.3 mg, yield 43%).

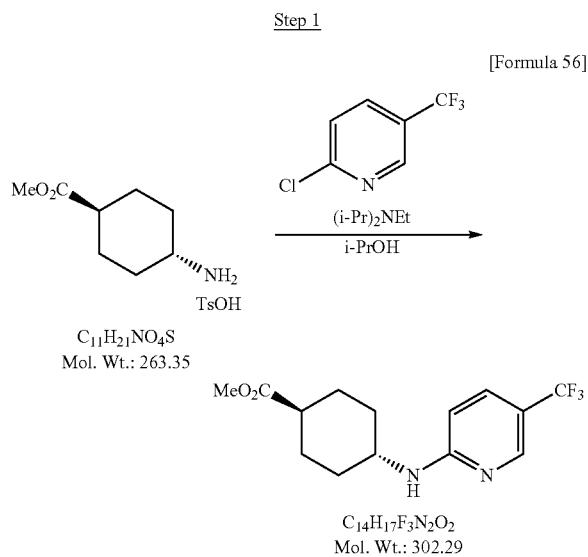
1H-NMR (DMSO-d6) δ ppm: 0.64 (q, 1H, J =11.6 Hz), 0.87 (d, 6H, J =6.0 Hz), 0.92-1.08 (m, 2H), 1.25 (s, 9H), 1.15-1.32 (m, 2H), 1.41 (m, 1H), 1.58-1.95 (m, 7H), 2.08 (t, 2H, J =11.6 Hz), 2.75-2.82 (m, 2H), 3.00 (m, 1H), 3.48-3.55 (m, 2H), 5.31 (m, 1H), 5.94 (d, 1H, J =8.5 Hz), 6.08-6.13 (m, 2H), 6.71 (d, 1H, J =8.5 Hz), 6.85 (t, 1H, J =8.5 Hz). Melting point: 161 to 162° C.

The compound obtained in Step 3 (500 mg, 2.01 mmol) was dissolved in chloroform (5 ml) and Dess-Martin periodinane (893 mg, 2.11 mmol) was added thereto. The mixture was stirred at room temperature for 1 hour. The deposit was

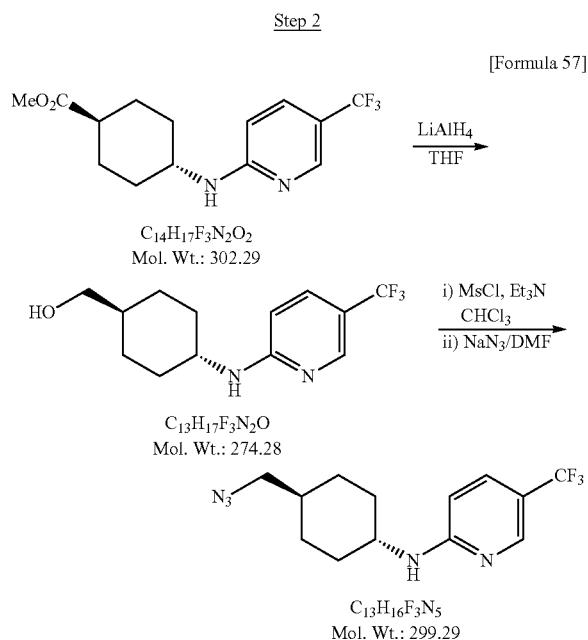
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Example 2

Synthesis of Compound (Ij-1)

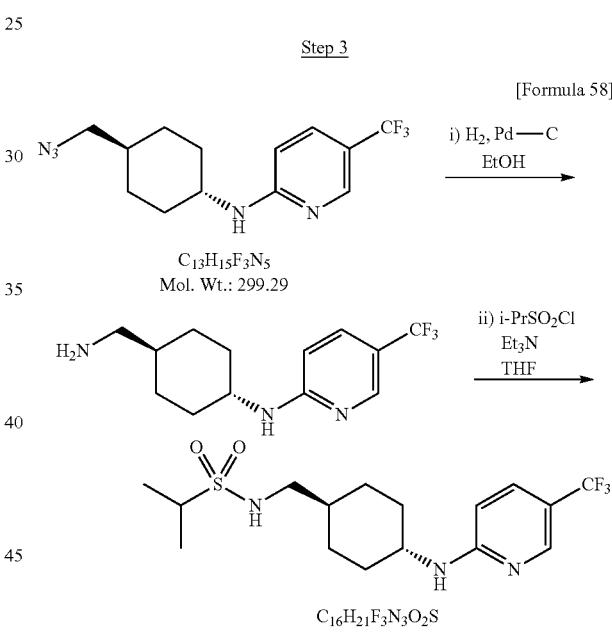


Amine (1.20 g, 3.64 mmol) and 2-chloro-5-trifluoromethylpyridine (727 mg, 4.01 mmol) was suspended in isopropanol (4 ml) and N,N-diisopropyl ethyl amine (1.87 ml, 10.9 mmol) was added thereto. After the mixture was in sealed tubes and the reaction was carried out by a microwave reactor for 1 hour at 160° C. The reactant was poured into water and extracted with ethyl acetate. The organic layer was washed with water and dried over sodium sulphate anhydrous. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography to give the desired ester (222 mg, 20% yield).



Ester obtained in Step 1 (207 mg, 0.685 mmol) was dissolved in tetrahydrofuran (3 ml). Lithium aluminum hydride

(31.1 mg, 0.822 mmol) was added thereto under ice-cooling and the mixture was stirred at room temperature for 0.5 hour. The reactant was poured into iced water and extracted with ethyl acetate. The organic layer was washed with water and dried over sodium sulphate anhydrous. The solvent was removed under reduced pressure to give alcohol. The obtained alcohol was dissolved in chloroform (3 ml). Triethylamine (0.28 ml, 2.04 mmol) was added thereto and methanesulfonyl chloride (0.12 ml, 1.64 mmol) was added dropwise under ice-cooling. The mixture was stirred at room temperature for 1 hour. The reactant was poured into water and extracted with ethyl acetate. The organic layer was washed with water and dried over sodium sulphate anhydrous. The solvent was removed under reduced pressure to give mesylate. The obtained mesylate was dissolved in dimethylformamide (3 ml) and sodium azide (221 mg, 3.40 mmol) was added thereto. The mixture was stirred for 3 hours at 100° C. The reactant was poured into water and extracted with ethyl acetate. The organic layer was washed with water and dried over sodium sulphate anhydrous. The solvent was removed under reduced pressure. The residue was purified by silica gel chromatography to give the desired azide (178 mg, 87% yield).



Azide (178 mg, 0.595 mmol) obtained in Step 2 was dissolved in ethanol (3 ml) and 10% Pd—C(30 mg) was added thereto to carry the hydrogenation reaction for 4 hours. Pd—C was removed by celite filtration and the filtrate was condensed under reduced pressure to give amine.

The obtained amine was dissolved in tetrahydrofuran (3 ml) and triethylamine (0.28 ml, 0.714 mmol) was added thereto. Isopropyl sulfonyl chloride (0.10 ml, 1.64 mmol) was added dropwise under ice-cooling and the mixture was stirred for 1 hour. The reactant was poured into water and extracted with ethyl acetate. The organic layer was washed with water and dried over sodium sulphate anhydrous. The solvent was removed under reduced pressure. The residue was purified by silica gel chromatography to give the desired compound (64.8 mg, 29% yield).

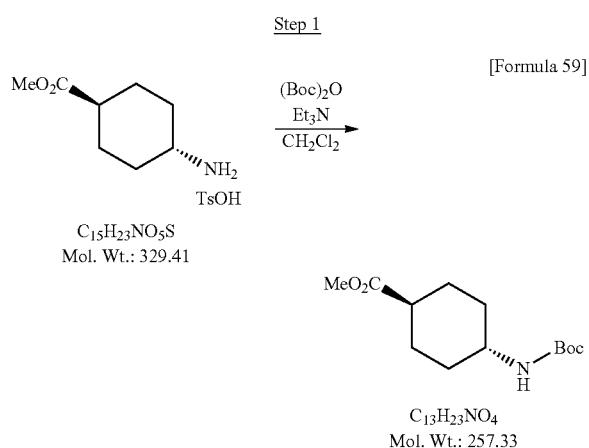
1H-NMR (DMSO-d6) δ: 0.92-1.06 (m, 2H), 1.10-1.25 (m, 2H), 1.22 (d, 6H, J=6.4 Hz), 1.38 (m, 1H), 1.76-1.84 (m, 2H),

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1.93-2.02 (m, 2H), 2.81 (t, 2H, $J=6.0$ Hz), 3.08-3.19 (m, 1H), 3.69 (m, 1H), 6.53 (d, 1H, $J=8.8$ Hz), 6.95 (t, 1H, $J=5.6$ Hz), 7.16 (d, 1H, $J=7.6$ Hz), 7.58 (d, 1H, $J=8.8$ Hz), 8.26 (s, 1H). Melting point: 155 to 156 °C.

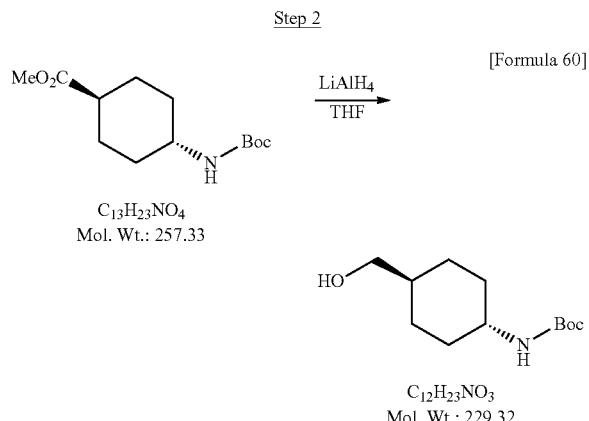
Example 3

Synthesis of Compound (Ij-1)



Amine (132 g, 401 mmol) was suspended in dichloromethane (1000 ml) under ice-cooling. Triethylamine (123 ml, 882 mmol) and (Boc)₂O (101 ml, 440 mmol) were sequentially added thereto and stirred for 10 minutes. After that, the mixture was stirred at room temperature for 2 hours and the solvent was removed. The residue was poured into aqueous citric acid (citric acid monohydrate 50 g in water 400 ml) to become pH4 and extracted with ethyl acetate. The organic layer was washed with water and dried over magnesium sulfate anhydrous. The solvent was removed under reduced pressure to quantitatively give the target compound.

reduced pressure to quantitatively give the target compound. ¹H-NMR (DMSO-d₆) δppm: 1.06-1.25 (m, 2H), 1.25-1.43 (m, 2H), 1.37 (s, 9H), 1.75-1.94 (m, 4H), 2.19 (tt, 1H, J=11.7, 3.9 Hz), 3.07-3.24 (m, 1H), 3.58 (s, 3H), 6.74 (d, 1H, J=6.6 Hz).

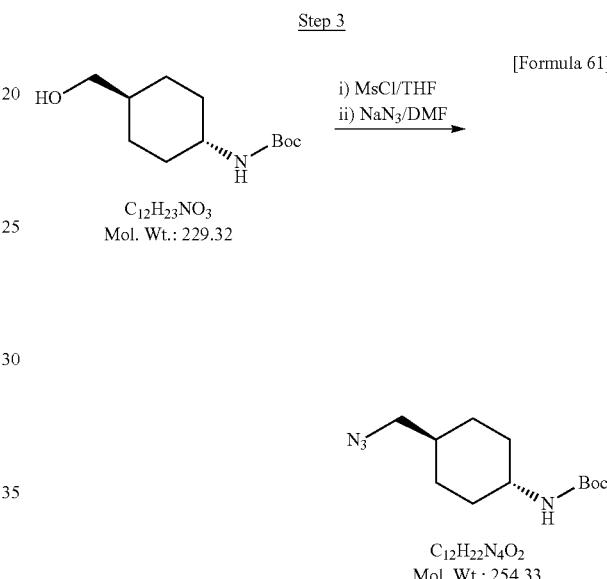


Lithium aluminum hydride (18.3 g, 483 mmol) was suspended in tetrahydrofuran (800 ml) and ester in tetrahydrofuran (300 ml) obtained in Step 1 was slowly added thereto

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under ice-cooling with stirring over 1 hour. The mixture was stirred under ice-cooling for 10 minutes and at room temperature for 2.5 hours. The reactant was ice-cooled and the mixture of water and tetrahydrofuran (1:1, 36 ml), 2N aqueous sodium hydroxide (18 ml) and water (18 ml) were sequentially added thereto. The mixture was stirred for 20 minutes and at room temperature for 1.5 hours. The deposit was removed by filtration, the filtrate was condensed under reduced pressure. Ethyl acetate and hexane was added to the residue. The precipitated crystals were collected with filtration to give the desired alcohol (79.5 g, 87% yield)(through Step 1 to 2).

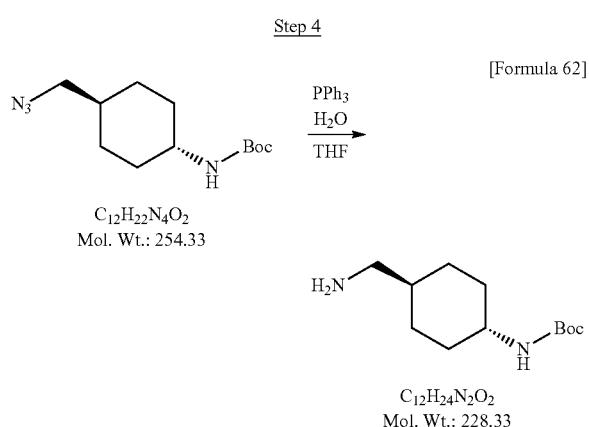
1H-NMR (DMSO-d₆) δ ppm: 0.78-1.00 (m, 2H), 1.00-1.32 (m, 3H), 1.37 (s, 9H), 1.65-1.84 (m, 4H), 3.04-3.24 (m, 3H), 4.32-4.42 (m, 1H), 6.66 (d, 1H, J=7.8 Hz).



Alcohol (79.5 g, 347 mmol) was dissolved in tetrahydrofuran (800 ml). Triethylamine (72.5 ml, 520 mmol) and methanesulfonyl chloride (32.2 ml, 416 mmol) were sequentially added thereto under ice-cooling with stirring and the mixture was stirred for 1.5 hours. The reactant was poured into aqueous citric acid (citric acid monohydrate 30 g in water 500 ml) to become pH4 and extracted with ethyl acetate. The organic layer was washed with water and dried over magnesium sulfate anhydrous. The solvent was removed under reduced pressure. The crystal deposited in the removal process was collected by filtration and washed with hexane to give mesylate (100 g). The obtained mesylate was dissolved in dimethylformamide (100 ml) and sodium azide (63.7 g, 980 mmol) was added thereto and reacted at 80°C. for 2 hours. The reactant was poured into water and extracted with ethyl acetate. The organic layer was washed with water and dried over magnesium sulfate anhydrous and the solvent was removed under reduced pressure to quantitatively give the desired azide (the crude weight is 85.4 g).

⁶⁵ ¹H-NMR (DMSO-d₆) δppm: 0.90-1.21 (m, 4H), 1.32-1.50 (m, 1H), 1.37 (s, 9H), 1.65-1.84 (m, 4H), 3.06-3.24 (m, 3H), 6.71 (d, 1H, J=8.1 Hz).

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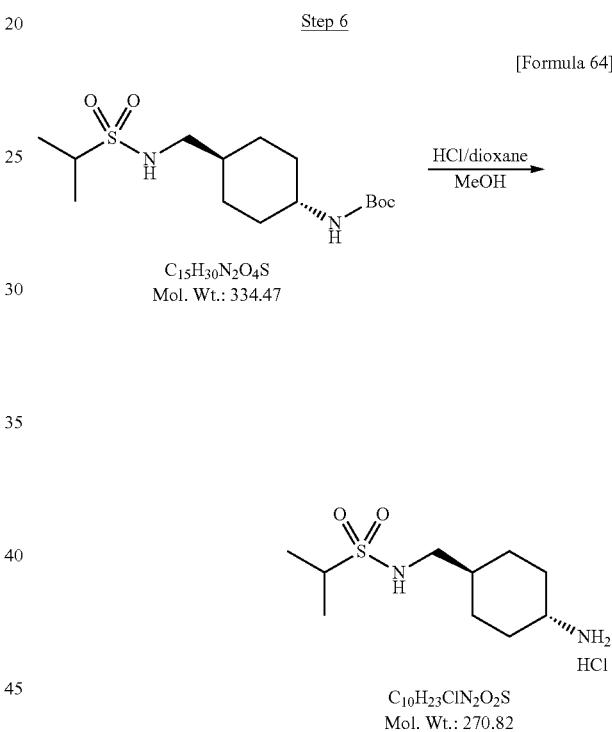


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Amine (37.5 g, 164 mmol) was suspended in tetrahydrofuran (400 ml). Triethylamine (91.7 ml, 656 mmol) and isopropyl sulfonyl chloride (32.2 ml, 416 mmol) were slowly and sequentially added thereto at -55 to -40° C. with stirring. 5 The mixture was stirred for 6 hours with gradually warming to 0° C. The reactant was poured into the ice-cooled dilute aqueous acid and extracted with ethyl acetate. The organic layer was washed with water and dried over magnesium sulfate anhydrous. The solvent was removed under reduced pressure and isopropyl ether was added to the residue. The precipitated crystals were collected with filtration and washed with isopropyl ether to give the desired sulfonamide (43.1 g, 79% yield).

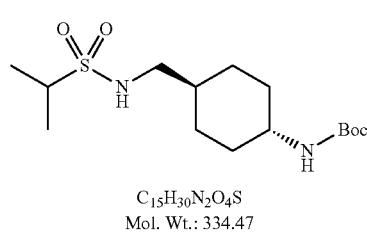
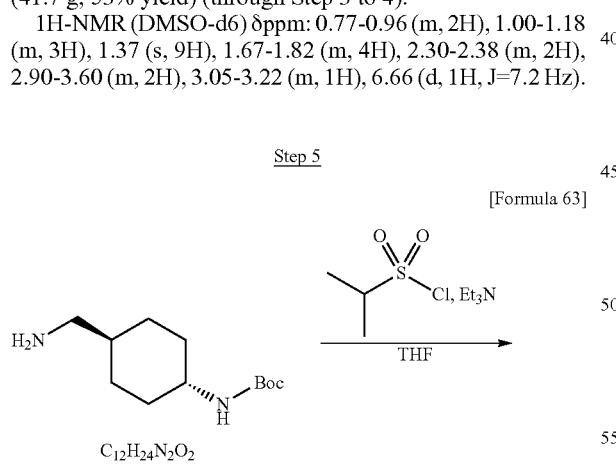
10 $^1\text{H-NMR}$ (DMSO-d6) δ ppm: 0.79-0.98 (m, 2H), 1.00-1.36 (m, 3H), 1.20 (d, 6H, J =6.6 Hz), 1.37 (s, 9H), 1.70-1.84 (m, 4H), 2.72-2.80 (m, 2H), 3.04-3.22 (m, 2H), 6.68 (d, 1H, J =8.1 Hz), 6.94 (t, 1H, J =6.0 Hz).

15 [Formula 64]



Azide obtained in Step 3 was dissolved in tetrahydrofuran (900 ml) at room temperature. Triphenylphosphine (103 g, 392 mmol) and water (90 ml) were sequentially added thereto and stirred at 80° C. for 1.5 hours. The solvent (770 ml) was removed and water (300 ml), ethyl acetate (400 ml) and 2N hydrochloric acid (150 ml) were sequentially added to become pH 2.5 and liquid-liquid extraction was carried out. The organic layer was extracted with 2N hydrochloric acid and the water layer was added thereto. The mixture was washed with ethyl acetate and 2N sodium hydroxide was added to alkalinize and repeatedly extracted with ethyl acetate and chloroform. The organic layer was added thereto and dried over magnesium sulfate anhydrous. The solvent was removed under reduced pressure and hexane was added to the residue. The precipitated crystals were collected with filtration and washed with hexane to give the desired amine (41.7 g, 53% yield) (through Step 3 to 4).

1H-NMR (DMSO-d6) δ ppm: 0.77-0.96 (m, 2H), 1.00-1.18 (m, 3H), 1.37 (s, 9H), 1.67-1.82 (m, 4H), 2.30-2.38 (m, 2H), 2.90-3.60 (m, 2H), 3.05-3.22 (m, 1H), 6.66 (d, 1H, J =7.2 Hz).



Boc-protected amine (43.0 g, 128 mmol) was suspended in methanol (200 ml) and 4N hydrochloric acid in dioxane (96 ml, 384 mmol) was added thereto under ice-cooling with stirring for 20 minutes and at room temperature for 3 hours. The reactant was ice-cooled and isopropyl ether (220 ml) was added thereto. After stirring for 30 minutes, the precipitated crystals were collected with filtration and washed with isopropyl ether to give the desired amine hydrochloride (30.8 g, 89% yield).

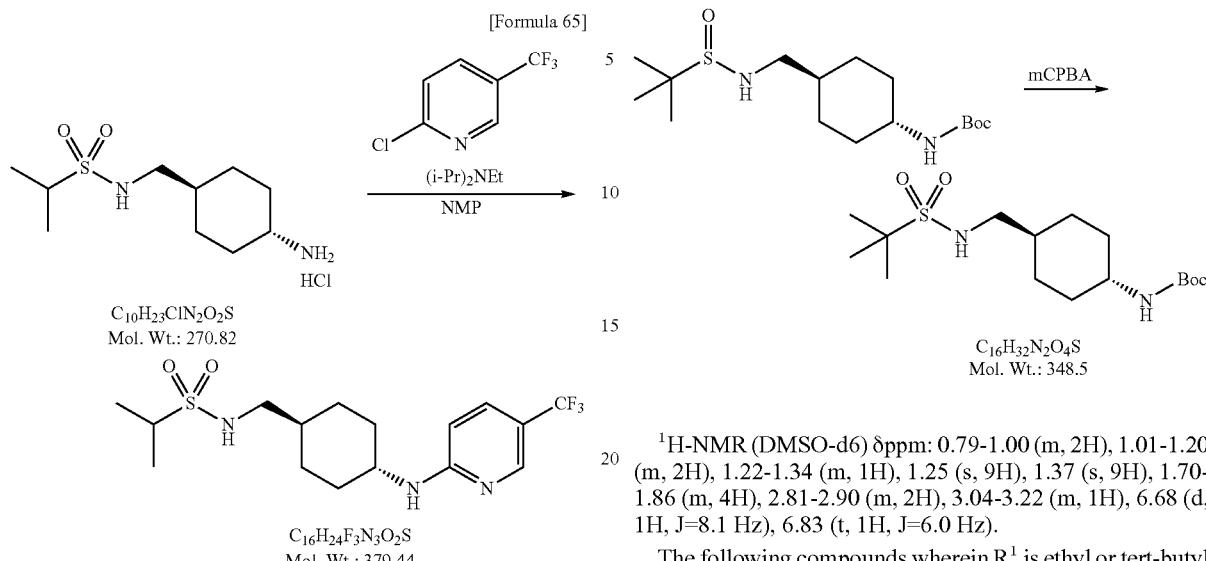
1H-NMR (DMSO-d6) δ ppm: 0.85-1.02 (m, 2H), 1.20 (d, 6H, J =6.6 Hz), 1.20-1.40 (m, 3H), 1.75-1.84 (m, 2H), 1.90-2.00 (m, 2H), 2.73-2.82 (m, 2H), 2.83-2.97 (m, 1H), 3.08-3.20 (m, 1H), 7.01 (t, 1H, J =5.7 Hz), 8.01 (s, 3H).

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Step 7

[Formula 67]



¹H-NMR (DMSO-d₆) δppm: 0.79-1.00 (m, 2H), 1.01-1.20 (m, 2H), 1.22-1.34 (m, 1H), 1.25 (s, 9H), 1.37 (s, 9H), 1.70-1.86 (m, 4H), 2.81-2.90 (m, 2H), 3.04-3.22 (m, 1H), 6.68 (d, 1H, J=8.1 Hz), 6.83 (t, 1H, J=6.0 Hz).

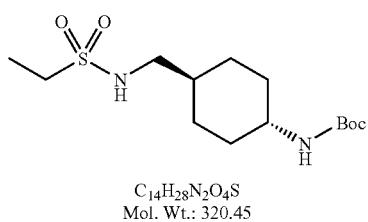
The following compounds wherein R¹ is ethyl or tert-butyl was obtained in Step 6 by using the above compound.

A compound wherein R¹ is ethyl.

Amine (190 mg, 0.700 mmol) and 2-chloro-5-trifluoromethylpyridin (1.27 g, 7.00 mmol) were suspended in N-methylpyrrolidone (4 ml) and N,N-diisopropyl ethyl amine (1.25 ml, 7.00 mmol) was added thereto. After the mixture was in sealed tubes and the reaction was carried out by a microwave reactor for 20 minutes at 210° C. The reactant was poured into water and extracted with ethyl acetate. The organic layer was washed with water and dried over sodium sulphate anhydrous. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography to give the desired Compound (Ij-1) (158 mg, 60% yield).

In Step 5, ethanesulfonyl chloride instead of isopropyl sulfonyl chloride was reacted to give the following compound wherein R¹ is ethyl.

[Formula 66]



¹H-NMR (DMSO-d₆) δppm: 0.80-0.98 (m, 2H), 1.02-1.18 (m, 2H), 1.17 (t, 3H, J=7.2 Hz), 1.22-1.34 (m, 1H), 1.37 (s, 9H), 1.68-1.82 (m, 4H), 2.68-2.78 (m, 2H), 2.96 (q, 2H, J=7.2 Hz), 3.04-3.22 (m, 1H), 6.68 (d, 1H, J=8.1 Hz), 6.94 (t, 1H, J=6.0 Hz).

In Step 5, tert-butyl sulfinylchloride instead of isopropyl sulfonyl chloride was reacted and the oxidation with mCPBA was carried out to give the following compound wherein R¹ is tert-butyl (WO2001037826, Example 3).

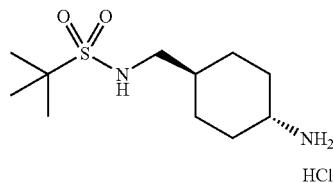
¹H-NMR (DMSO-d₆) δppm: 0.84-1.02 (m, 2H), 1.18 (t, 3H, J=7.5 Hz), 1.20-1.40 (m, 3H), 1.74-1.82 (m, 2H), 1.90-2.00 (m, 2H), 2.72-2.80 (m, 2H), 2.83-2.96 (m, 1H), 2.97 (q, 2H, J=7.5 Hz), 7.04 (t, 1H, J=6.0 Hz), 8.03 (s, 3H).

A compound wherein R¹ is tert-butyl

[Formula 66]

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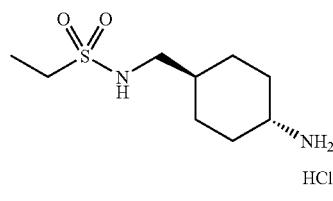
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¹H-NMR (DMSO-d₆) δppm: 0.84-1.04 (m, 2H), 1.16-1.38 (m, 3H), 1.26 (s, 9H), 1.74-1.84 (m, 2H), 1.92-2.02 (m, 2H), 2.82-2.98 (m, 3H), 6.90 (d, 1H, J=6.0 Hz), 8.01 (s, 3H).

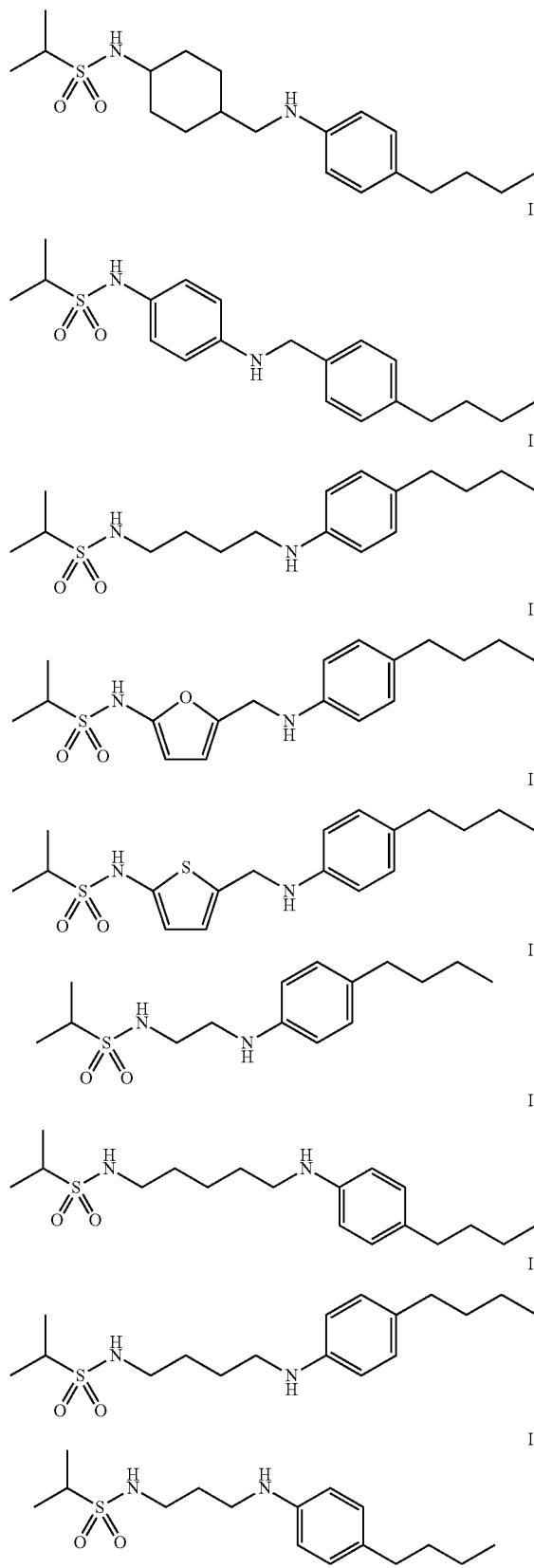
The following compounds synthesized in similar methods also include the present invention.

[Formula 68]



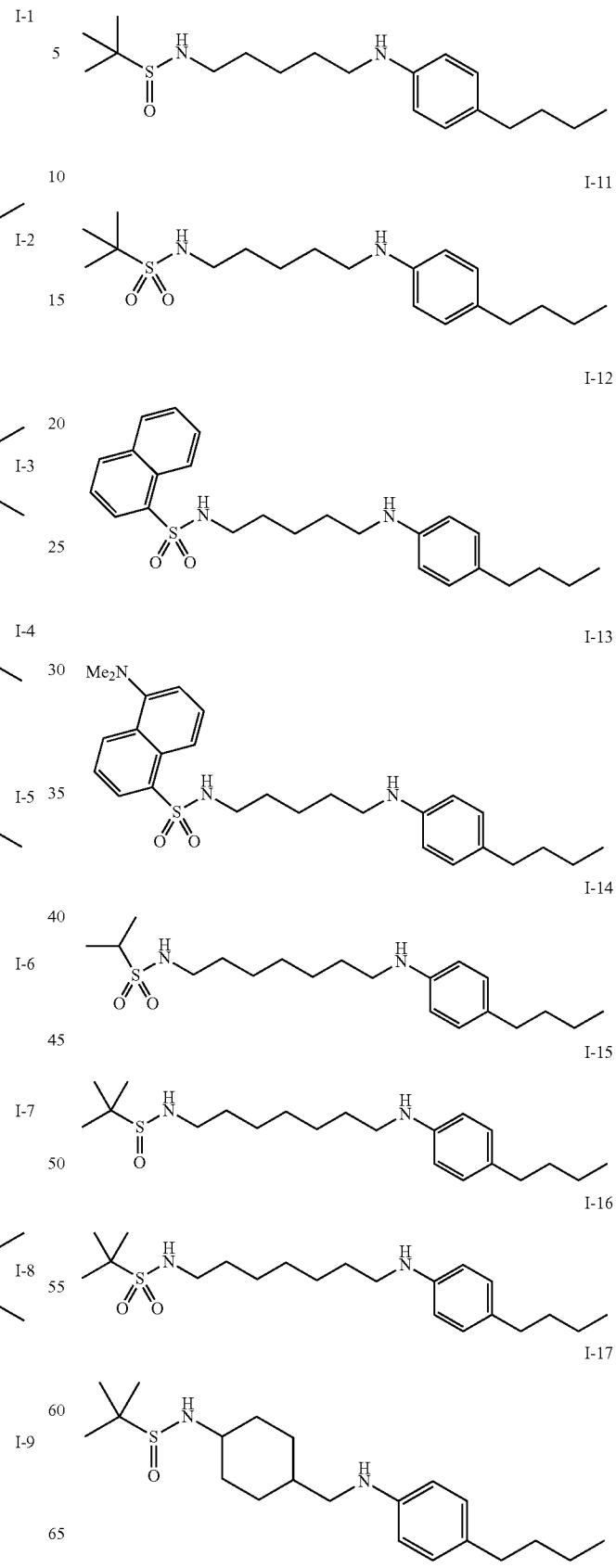
41

[Formula 70]

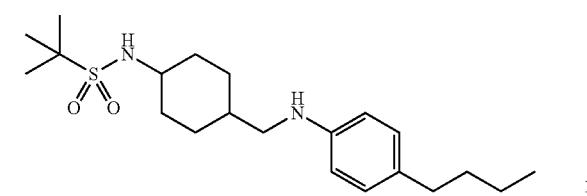
**42**

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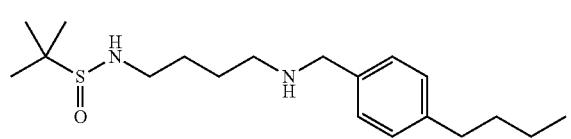
I-10



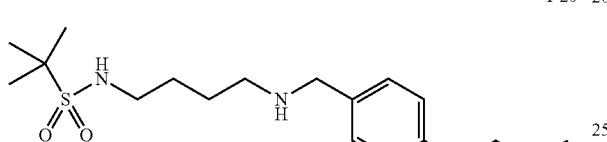
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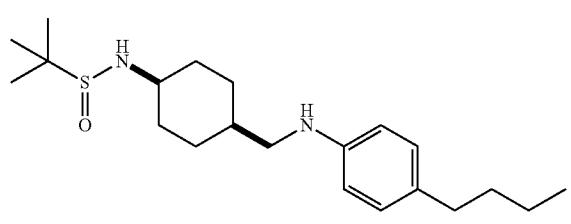
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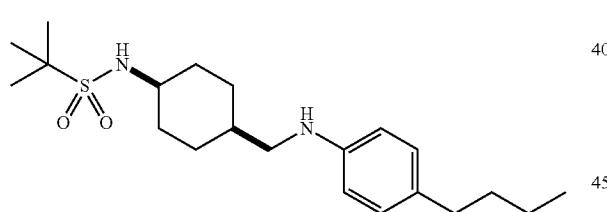
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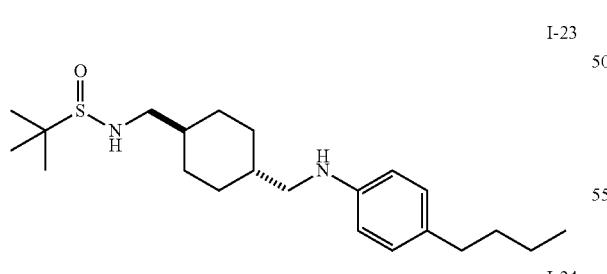
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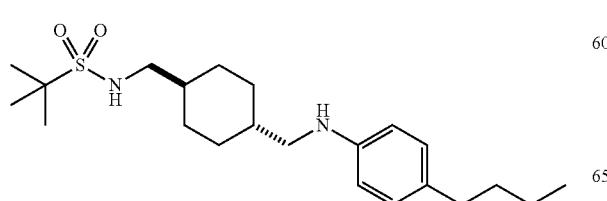
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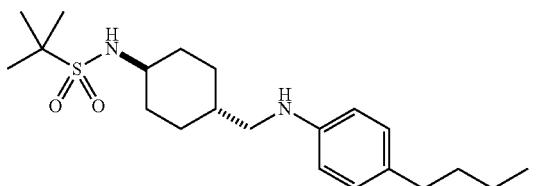


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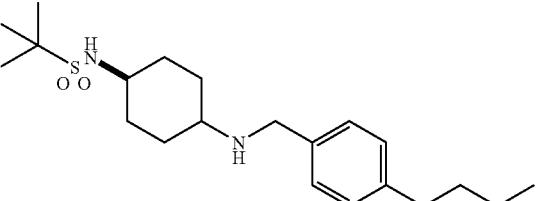
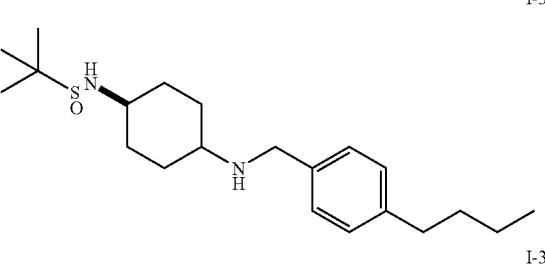
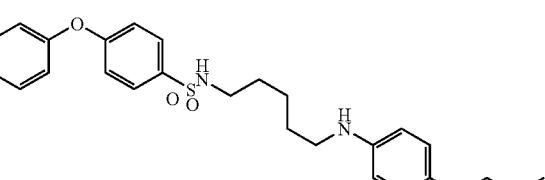
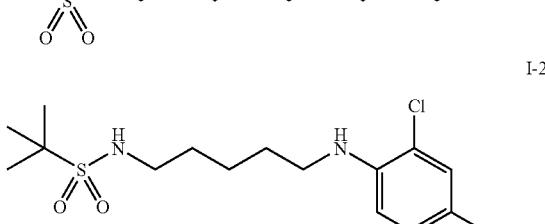
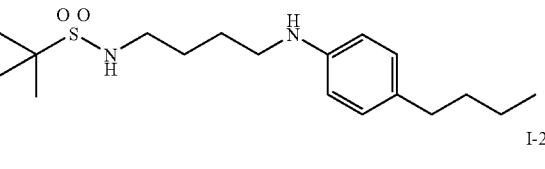
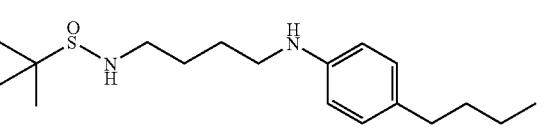


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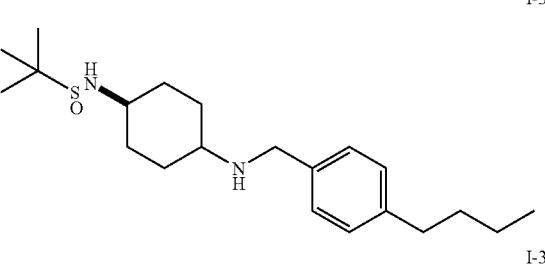
44
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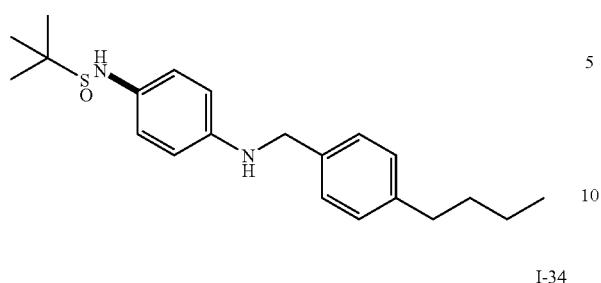


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[Formula 71]

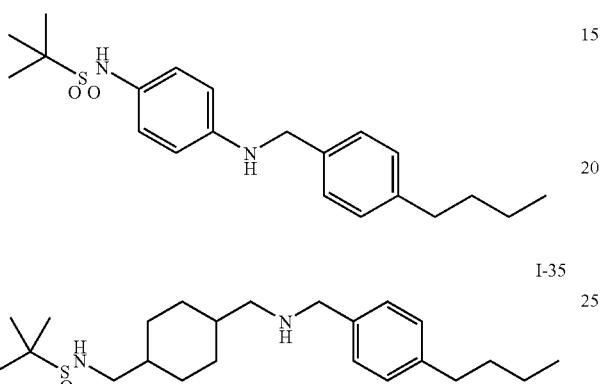
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I-33



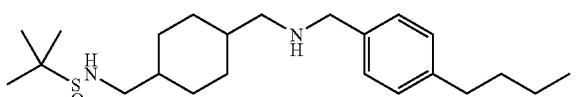
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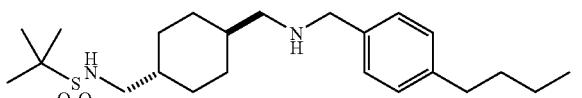
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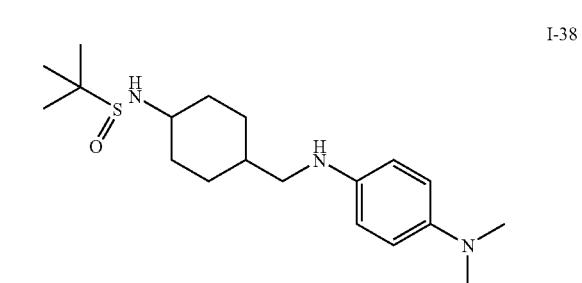
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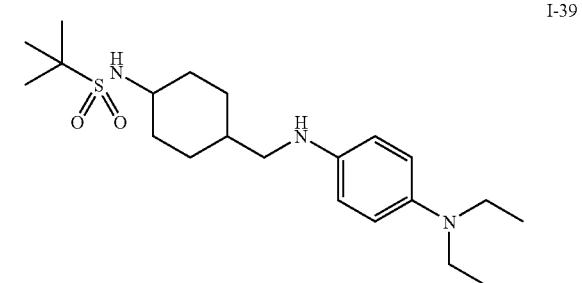
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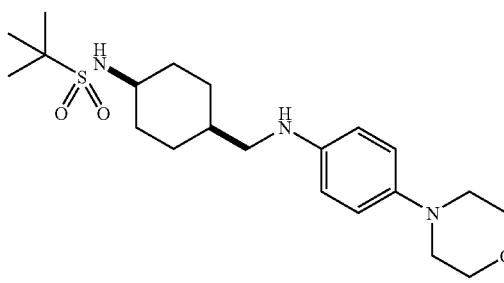
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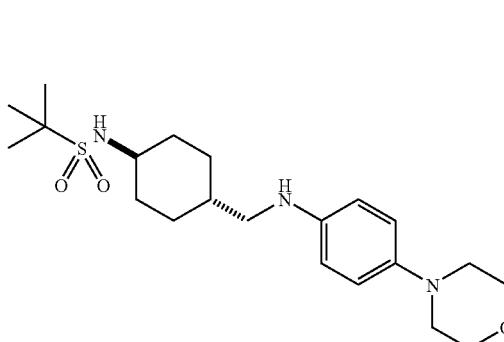
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46
-continued

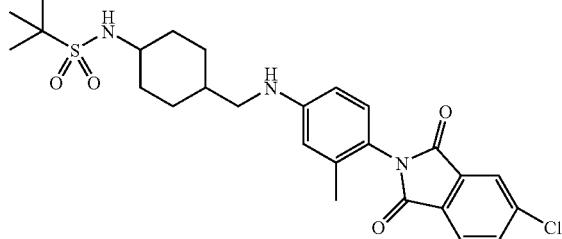
I-40



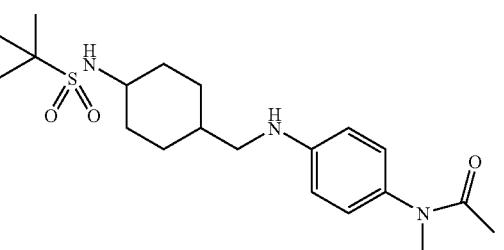
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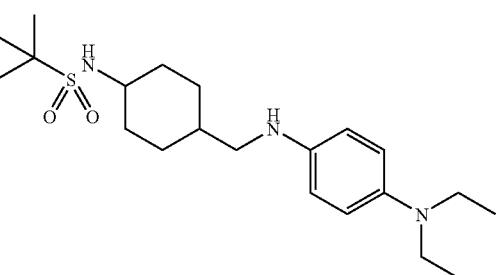
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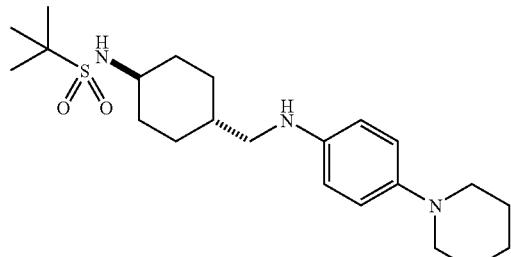
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47

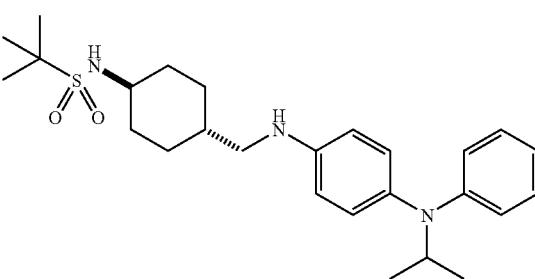
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[Formula 72]

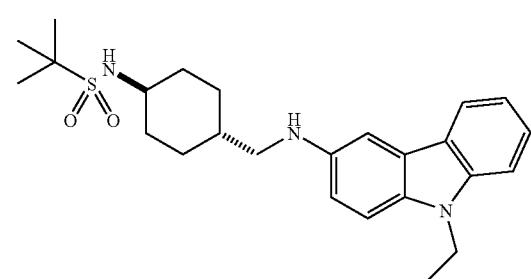


I-45

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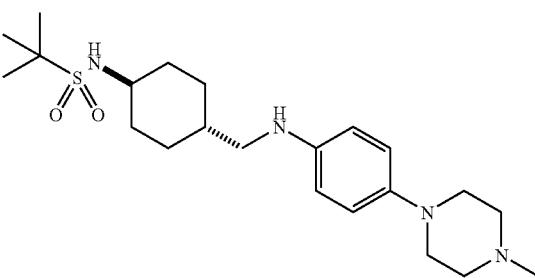


I-51

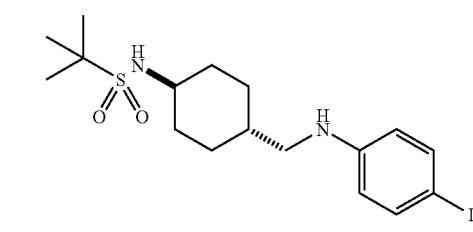


I-46

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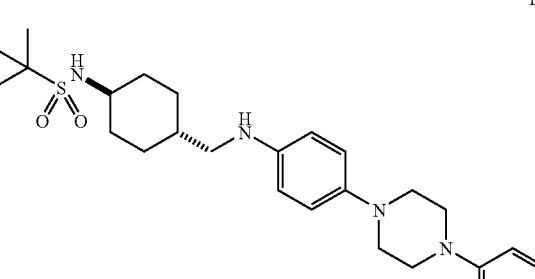


I-52

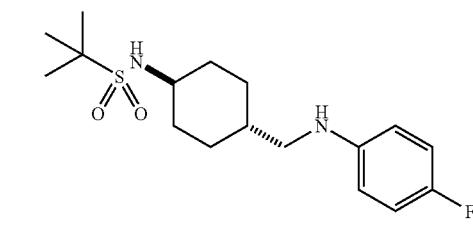


I-47

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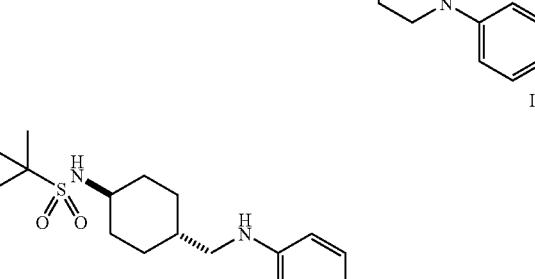


I-53

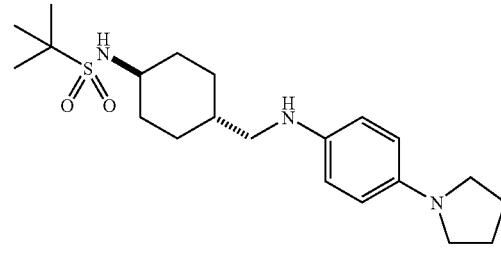


I-48

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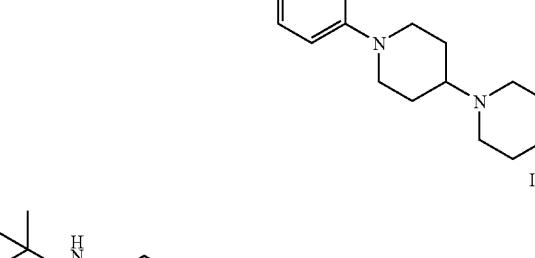


I-54

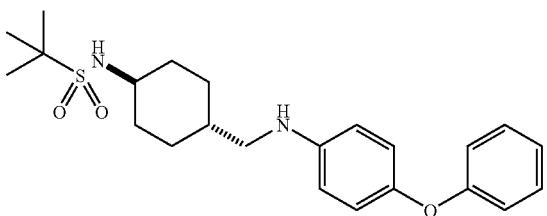


I-49

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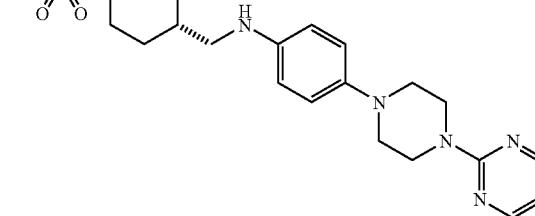


I-55



I-50

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I-56

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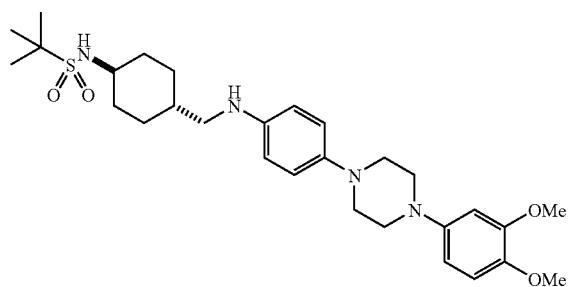
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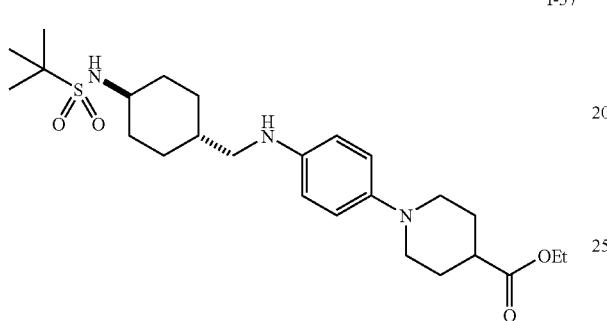
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49
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I-56

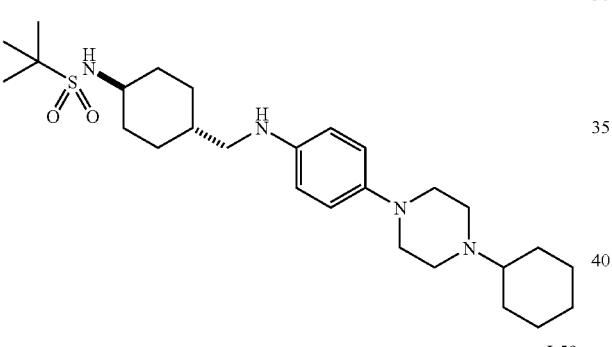
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I-57

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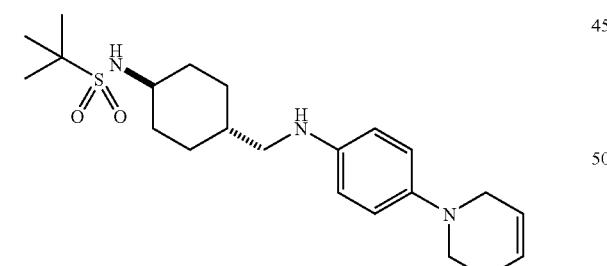
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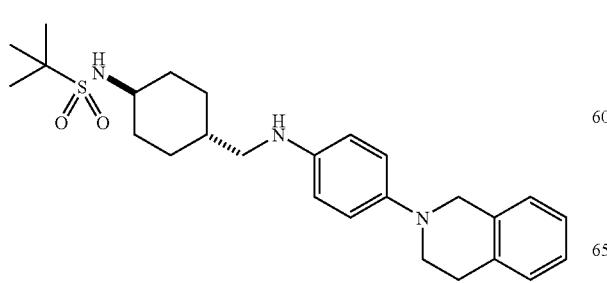
I-59



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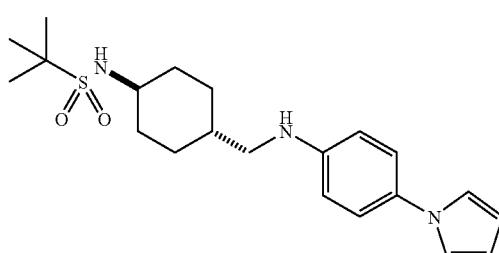


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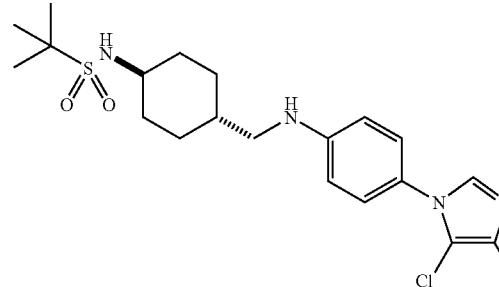
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I-62

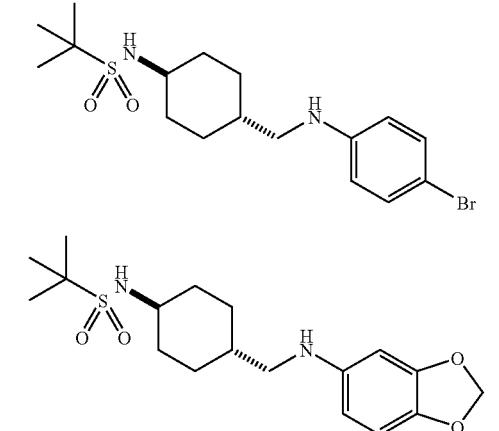
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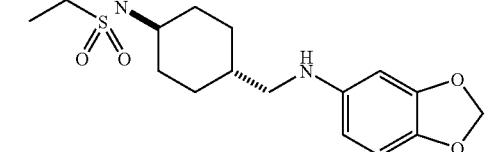
I-61



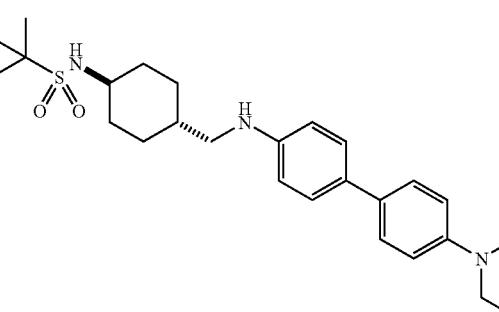
I-63



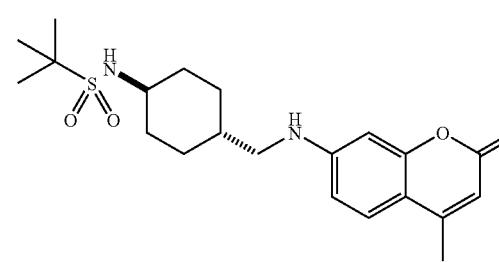
I-64



I-65



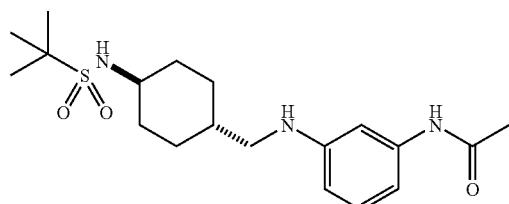
I-66



51

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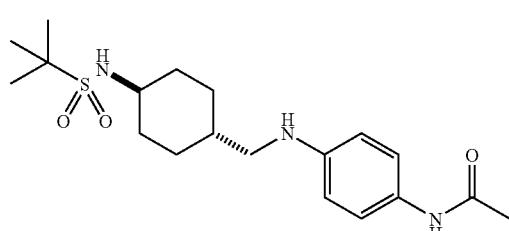
[Formula 73]



I-67

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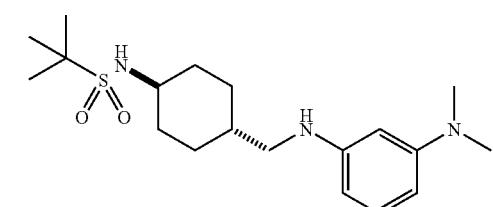
I-68



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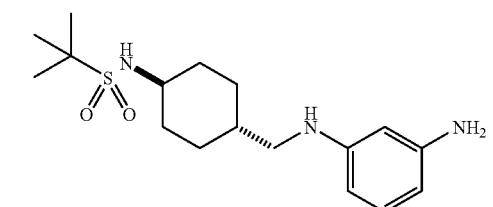
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I-69 25



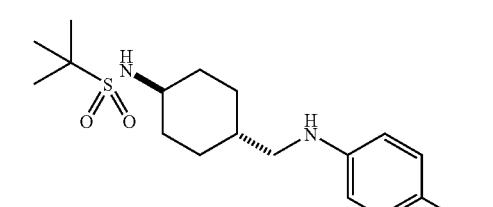
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I-70 35



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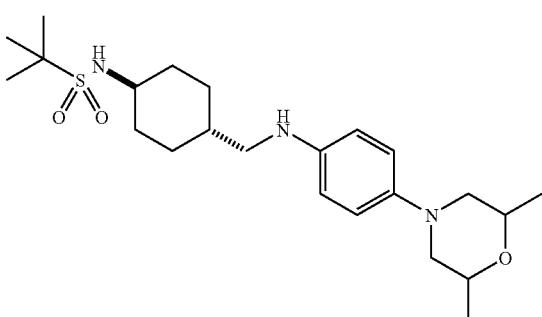
I-71 45



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I-72

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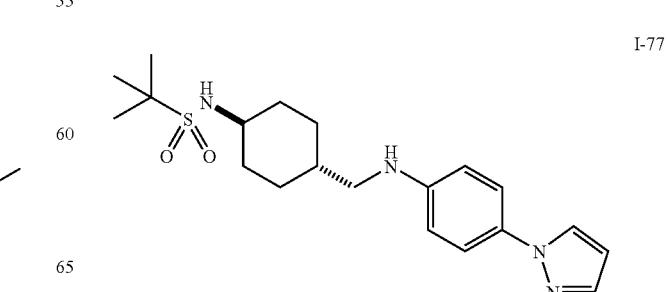
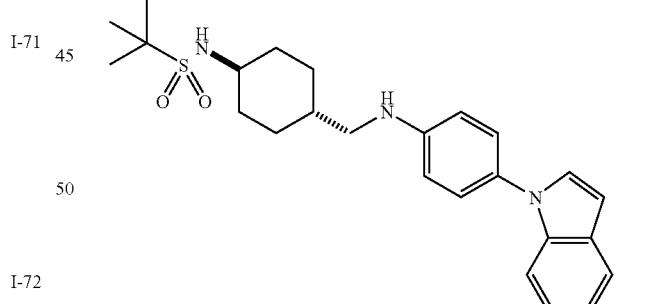
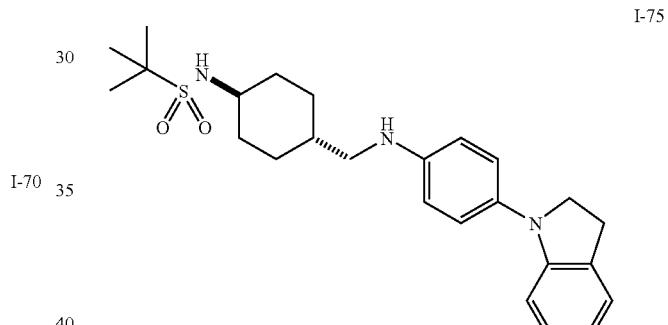
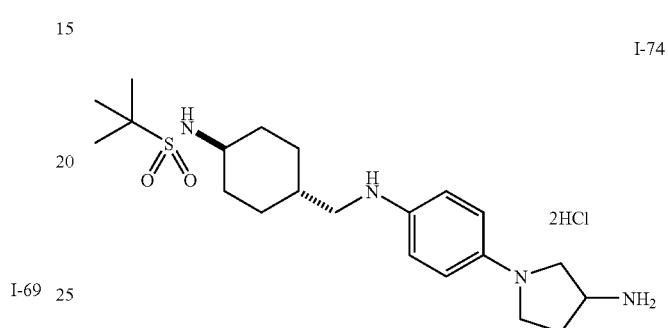
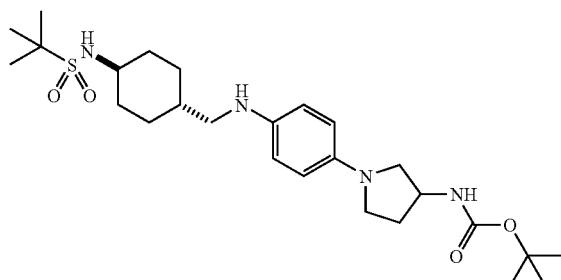
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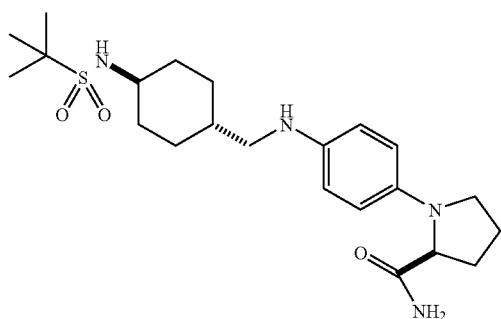
52

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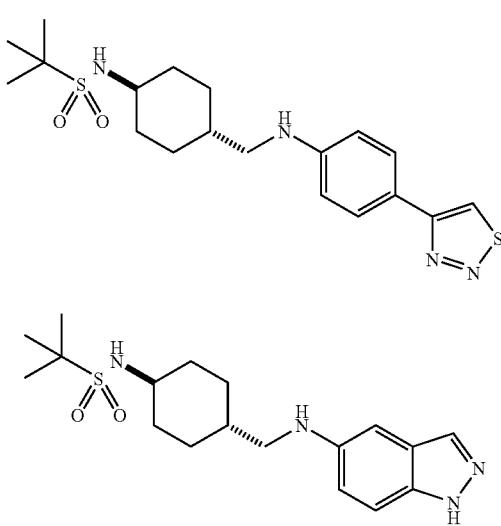
I-73



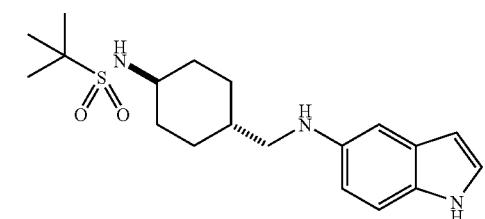
53
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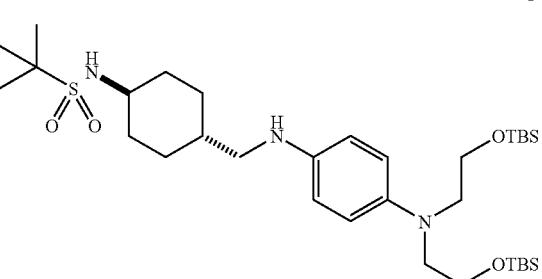
I-78



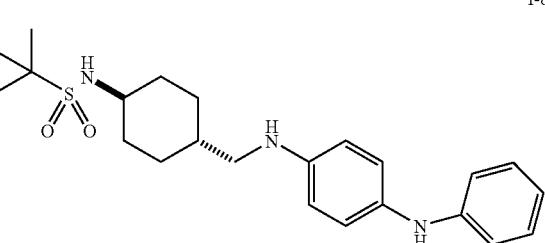
I-79 15



I-81 35

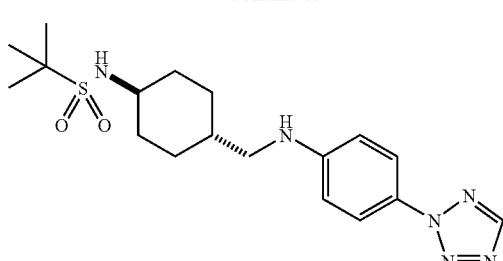


I-82 45

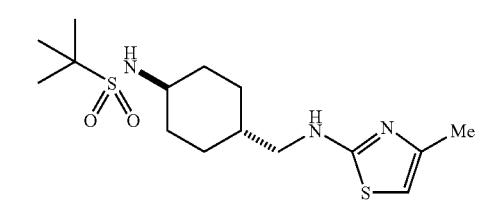


I-83

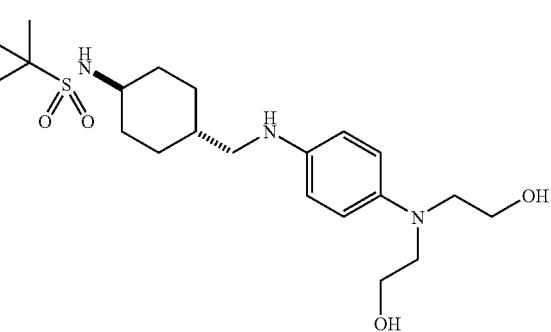
54
-continued



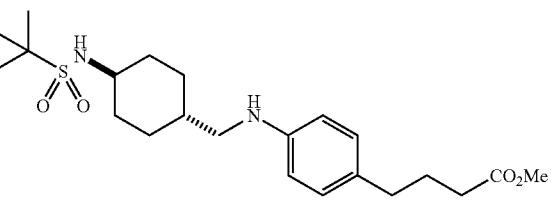
I-84



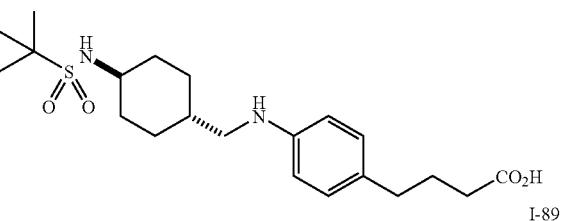
I-85



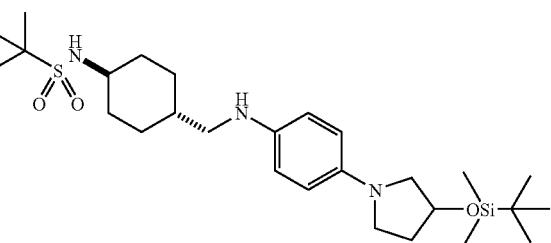
I-86



I-87



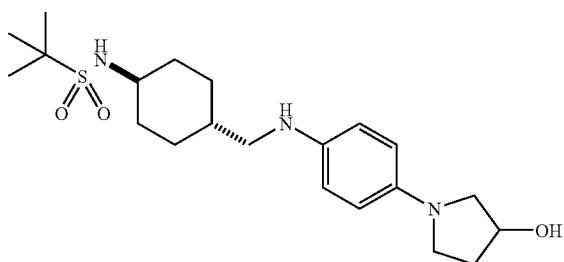
I-88



I-89

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-continued

I-90

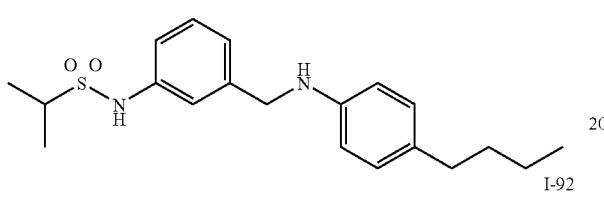


[Formula 74]

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I-91 15



I-92

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I-93

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I-94 40

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I-95

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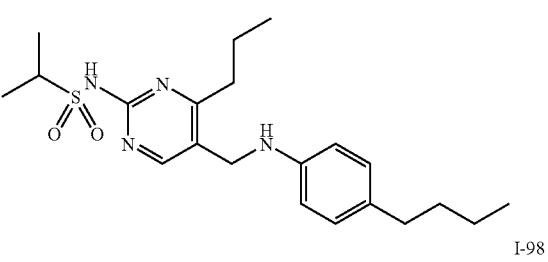
I-96

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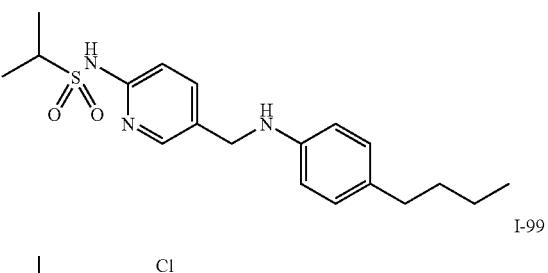
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56
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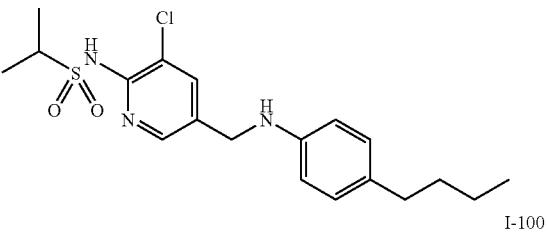
I-97



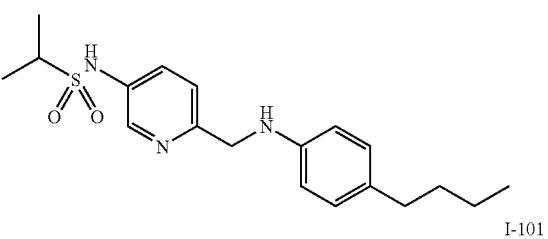
I-98



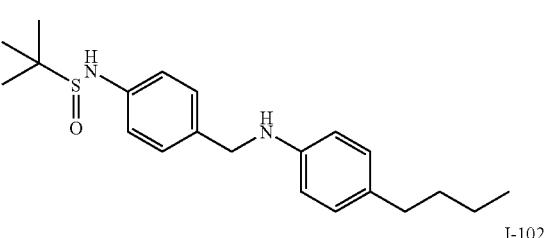
I-99



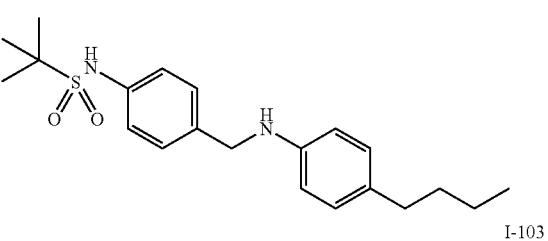
I-100



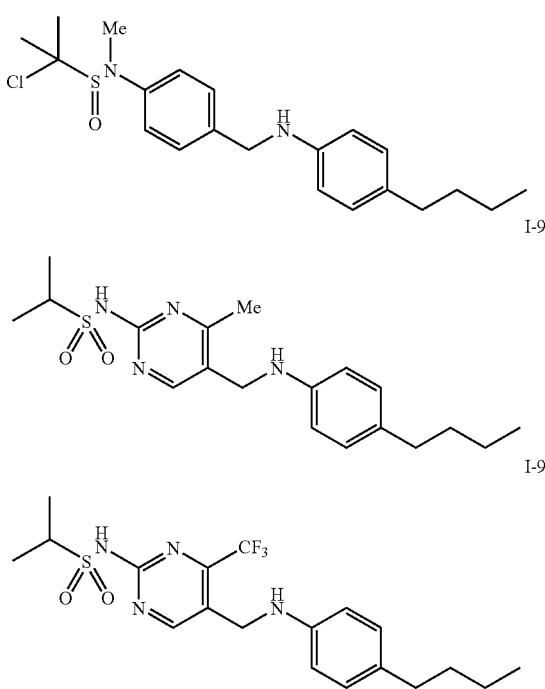
I-101



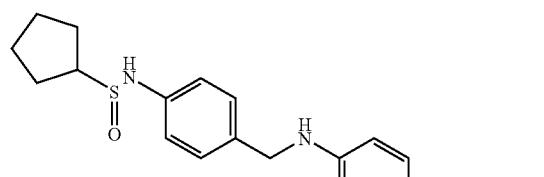
I-102



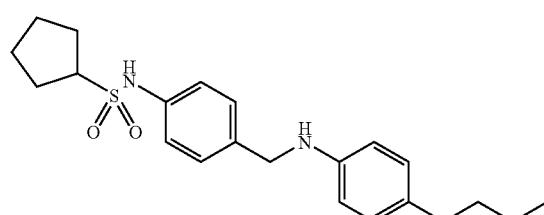
I-103



57
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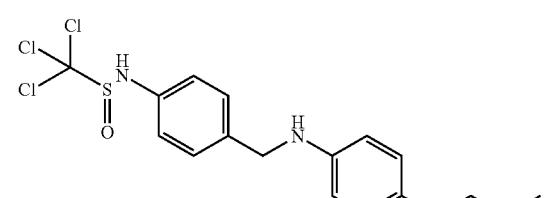
I-104



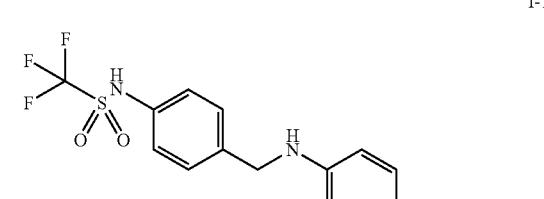
I-105



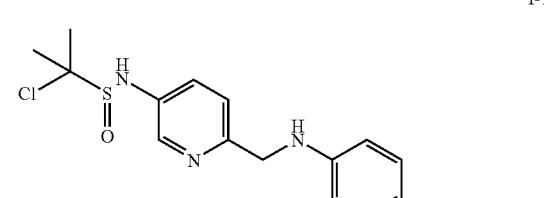
I-106 [Formula 75]



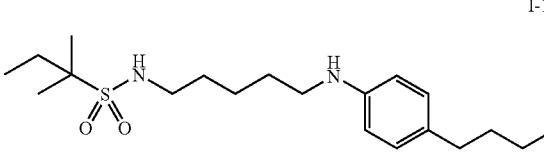
I-107



I-108

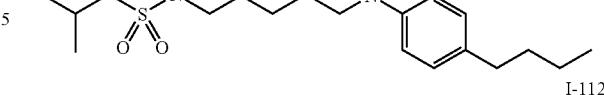


I-109

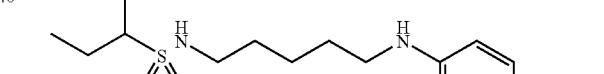
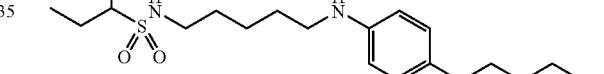
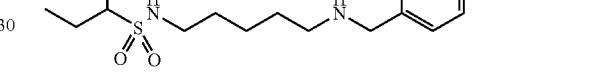
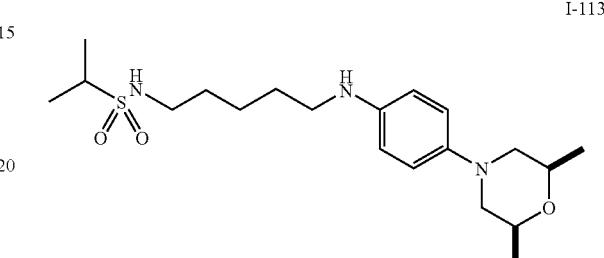
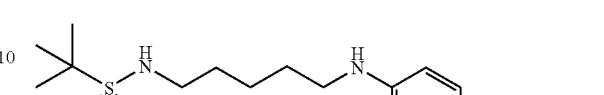
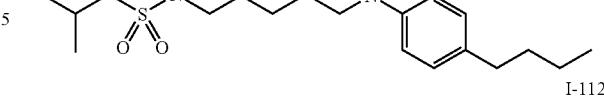


I-110

58
-continued

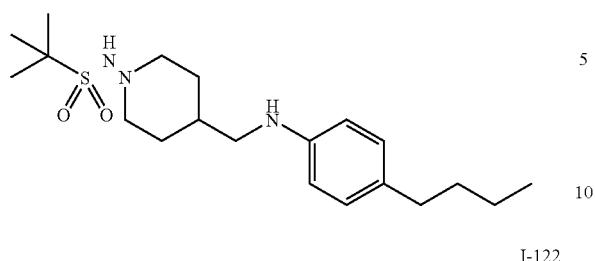


I-111



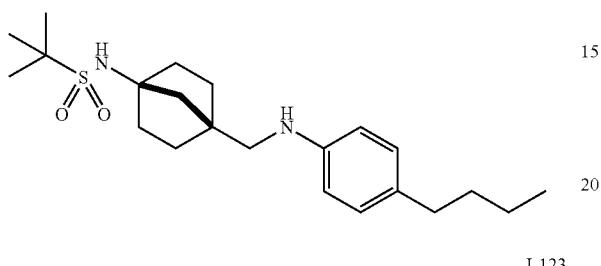
59
-continued

I-121



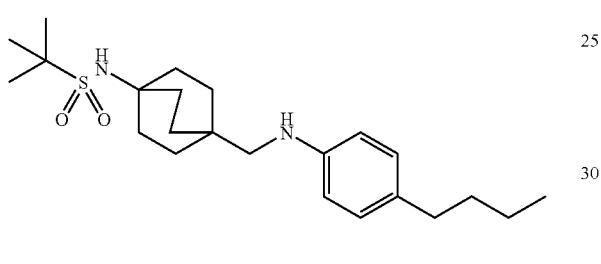
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I-122



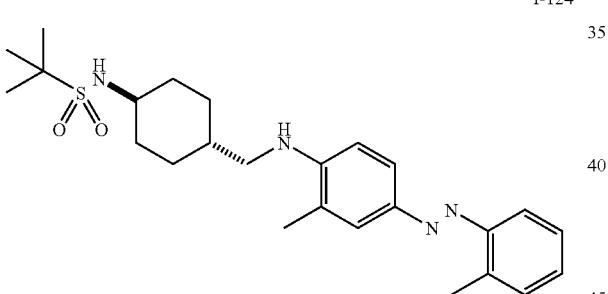
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I-123



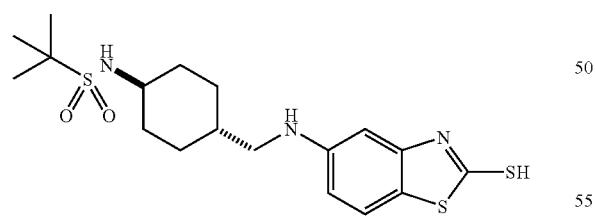
15

I-124



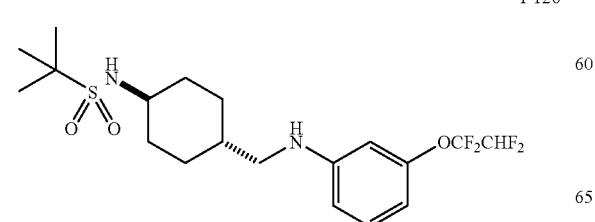
30

I-125



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I-126

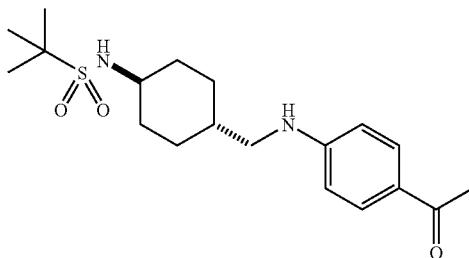


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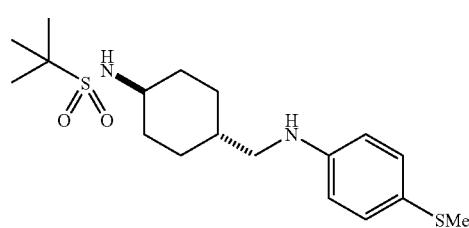
65

60
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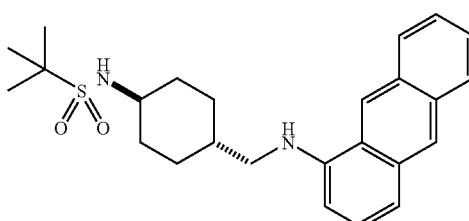
I-127



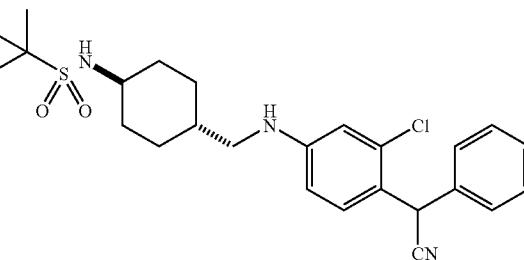
I-128



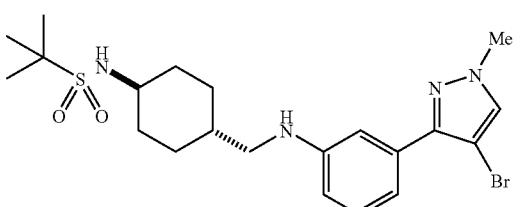
I-129



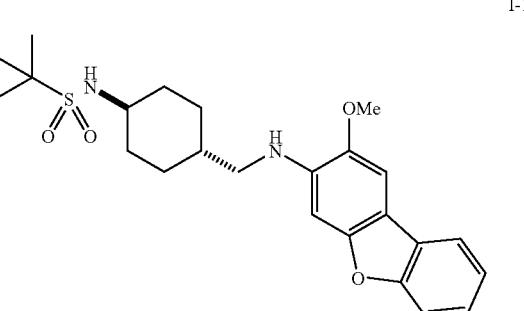
I-130



I-131

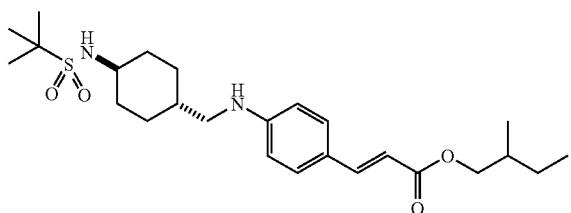


I-132



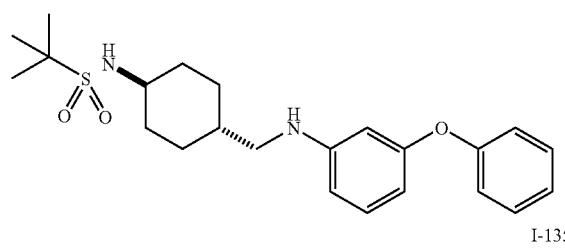
61
-continued

I-133 [Formula 76]



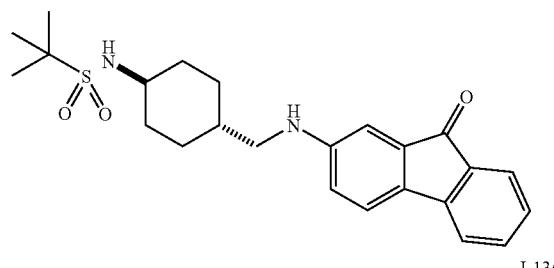
5

10



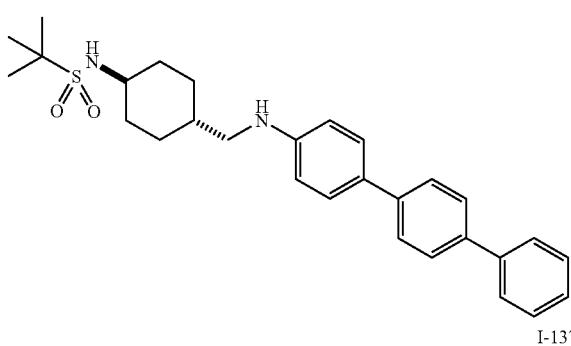
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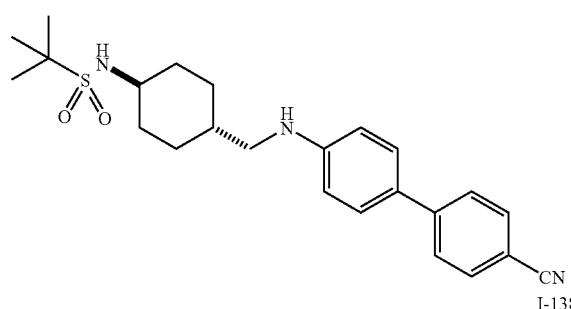
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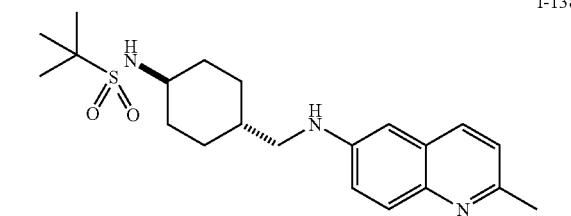
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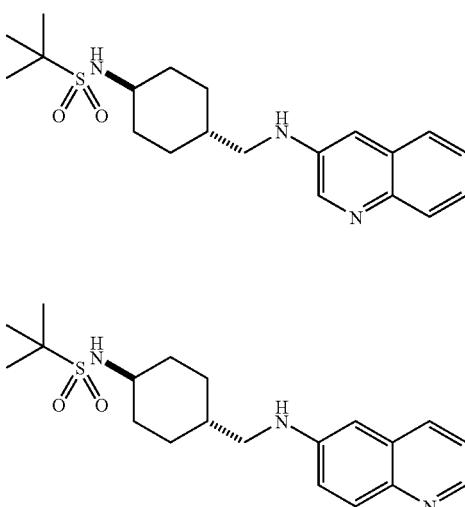
60



65

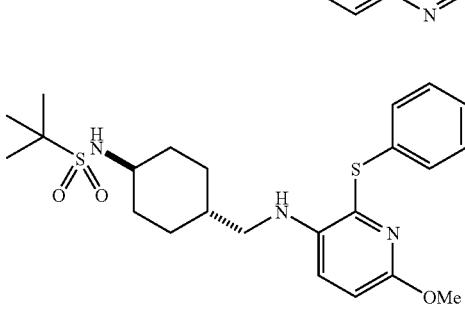
62
-continued

I-139



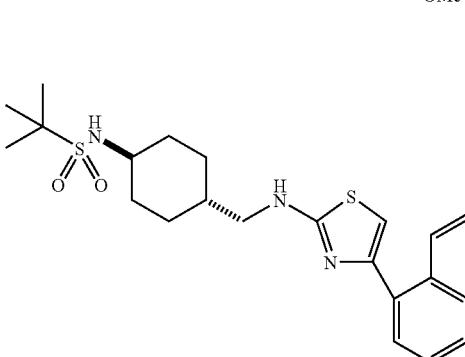
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20

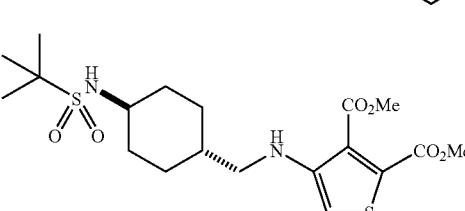
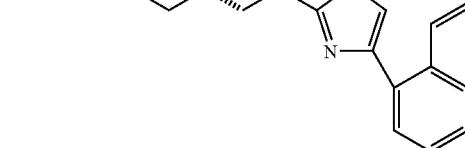


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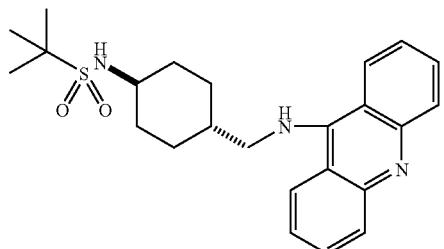
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65

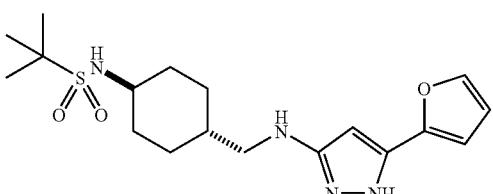
63
-continued

I-145



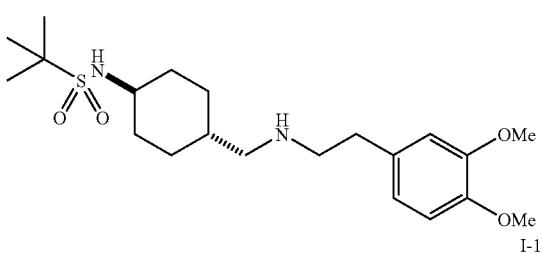
10

I-146



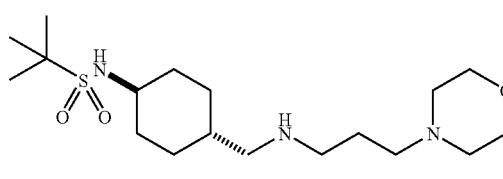
15

I-147



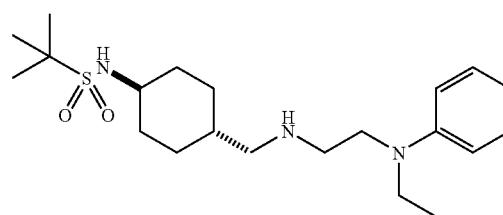
25

I-148



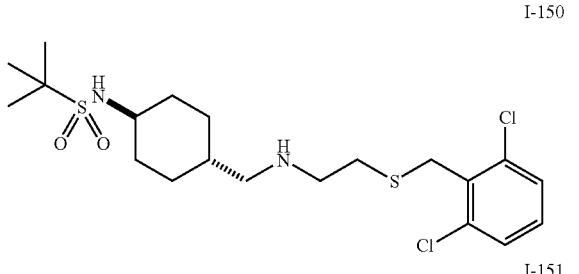
35

I-149



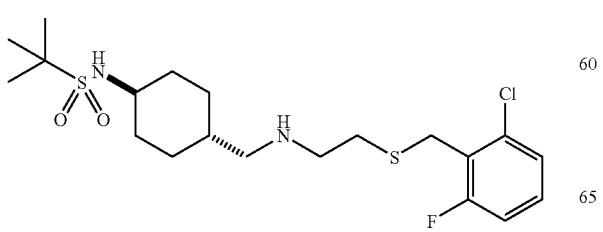
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I-150



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I-151

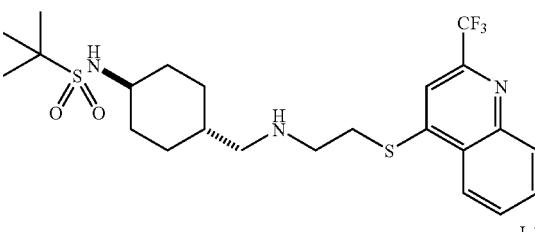


60

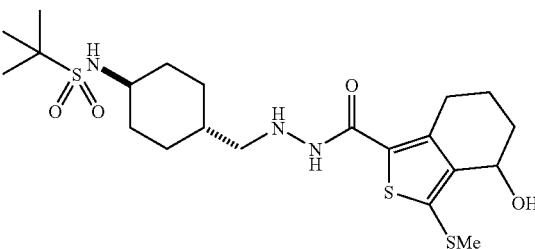
I-152

64
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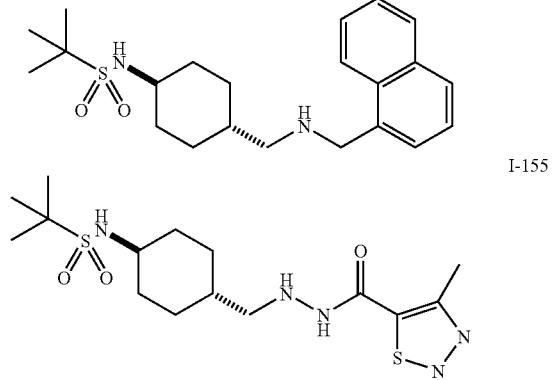
I-152



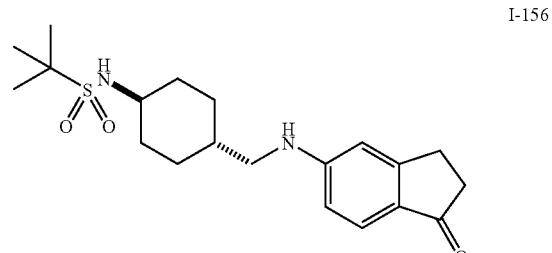
I-153



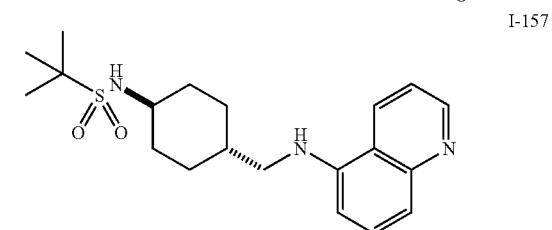
I-154



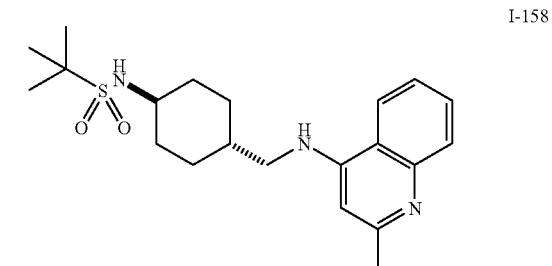
I-155



I-156

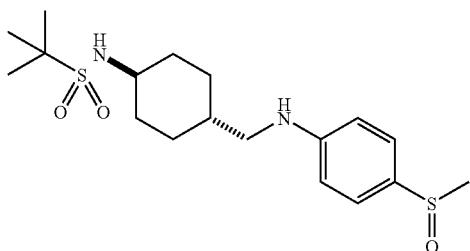


I-157

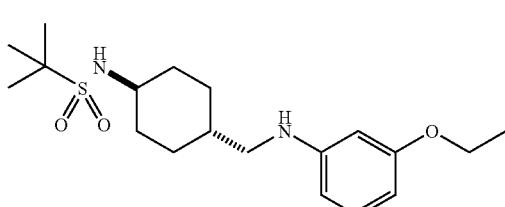


I-158

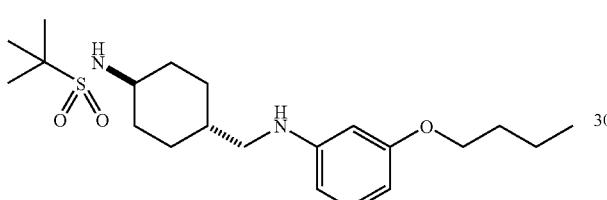
65
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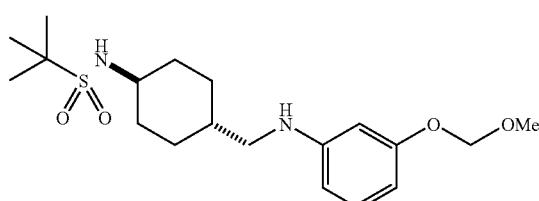
I-159



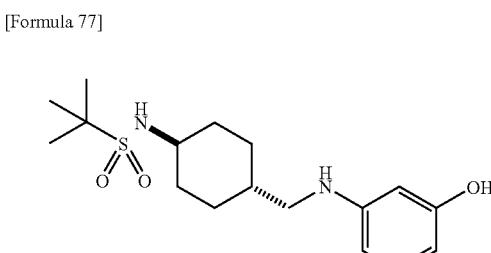
I-160



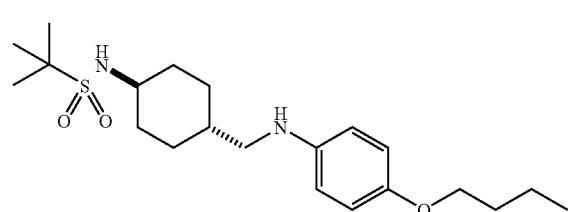
I-161



I-162

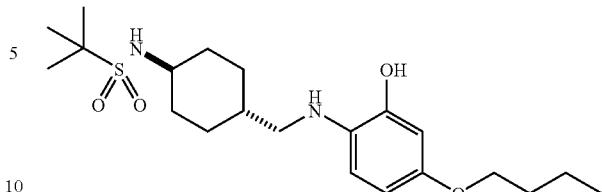


I-163

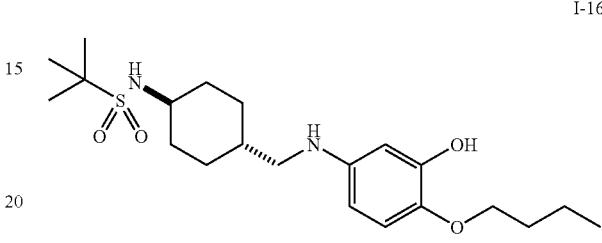


I-164

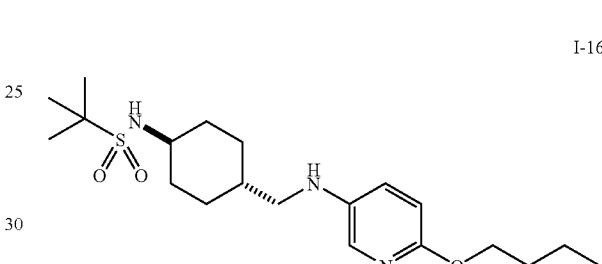
66
-continued



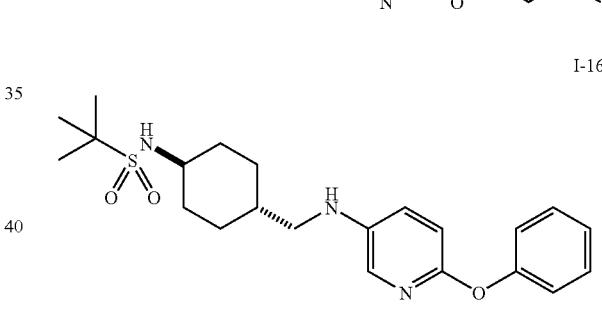
I-165



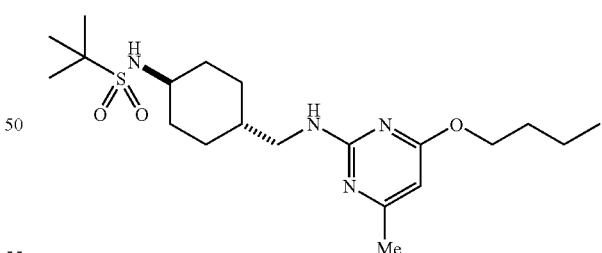
I-166



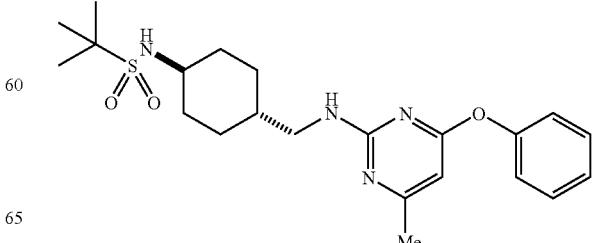
I-167



I-168



I-169

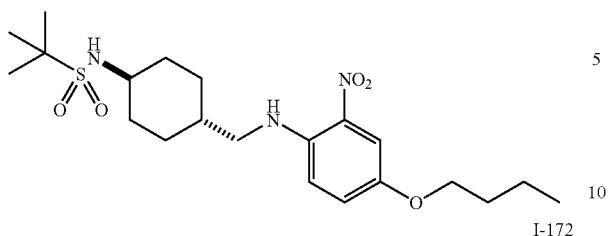


I-170

[Formula 77]

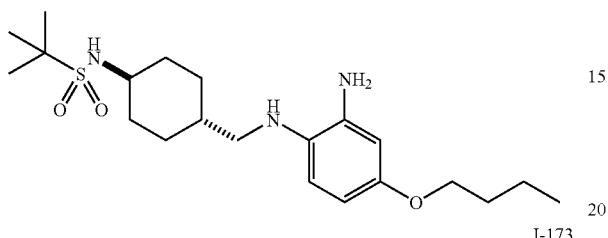
67
-continued

I-171



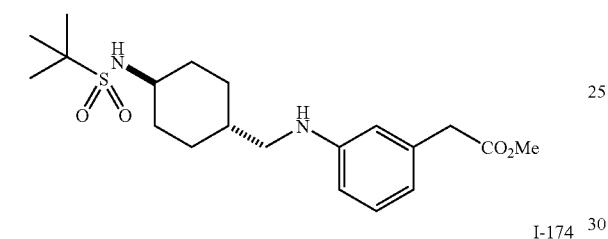
5

I-172



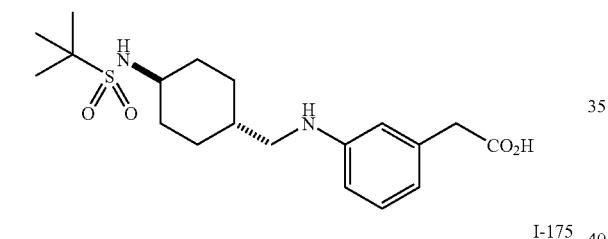
15

I-173



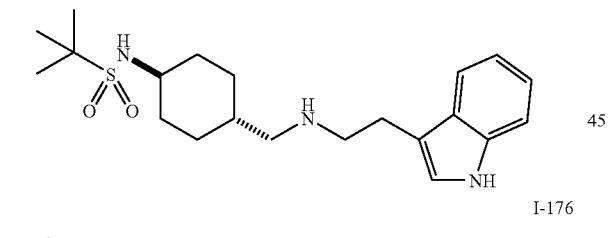
25

I-174



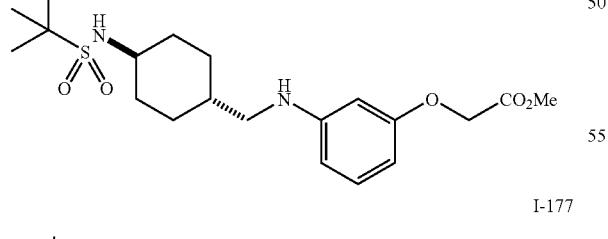
35

I-175



45

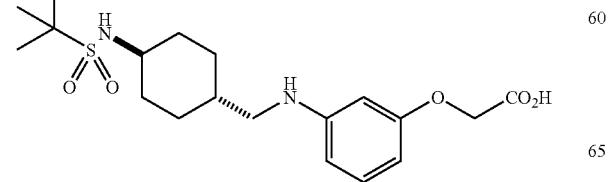
I-176



50

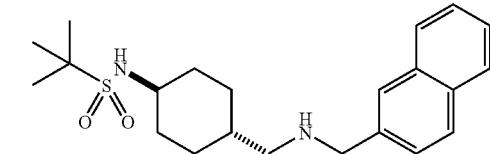
I-177

[Formula 78]

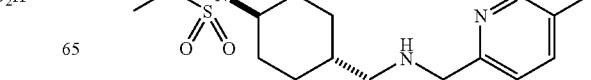


55

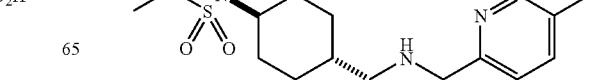
I-178



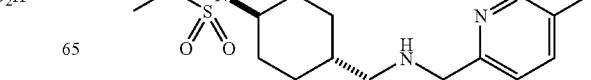
60



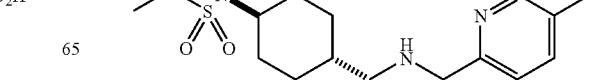
65



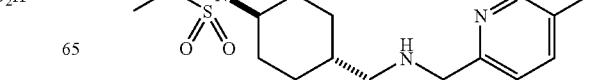
70



75



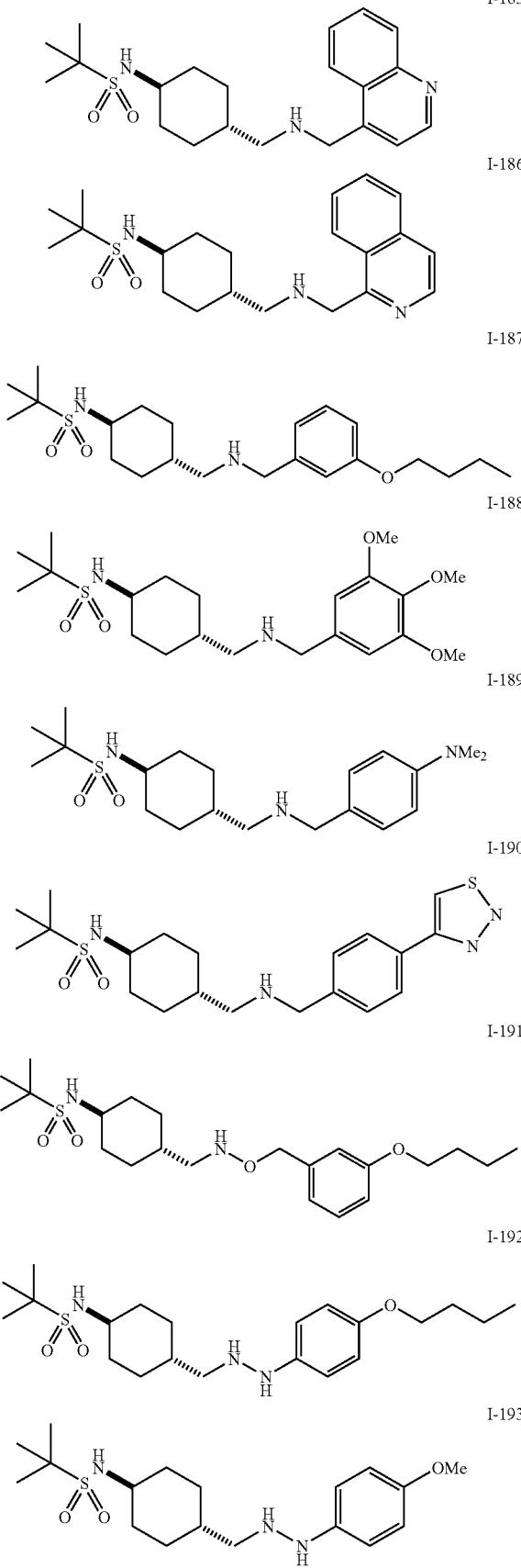
80



85

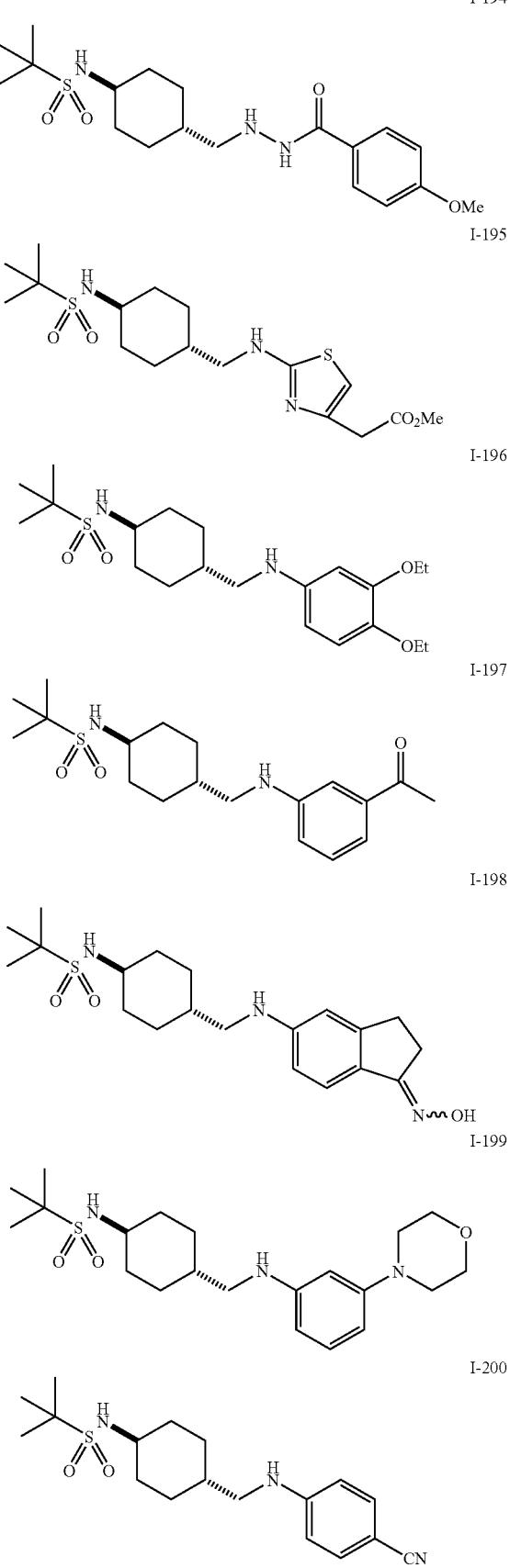
69
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I-185

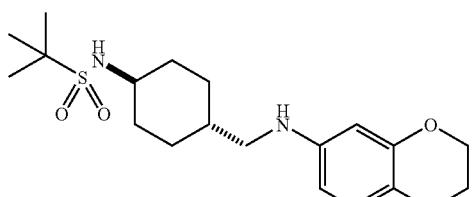


70
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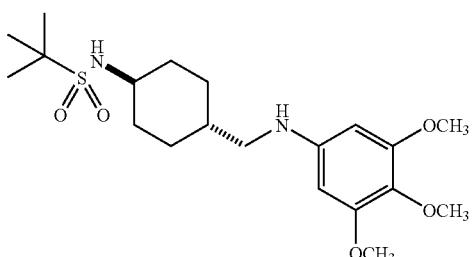
I-194



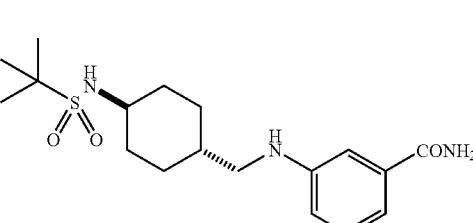
71
-continued



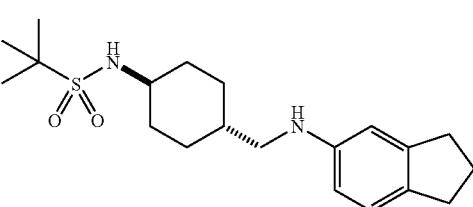
I-201



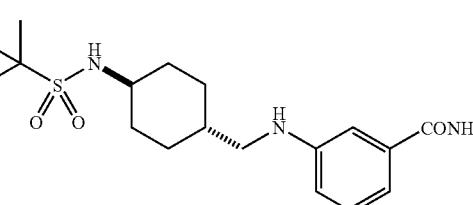
I-202



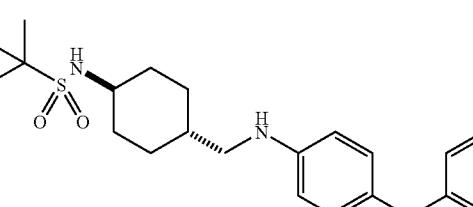
I-203



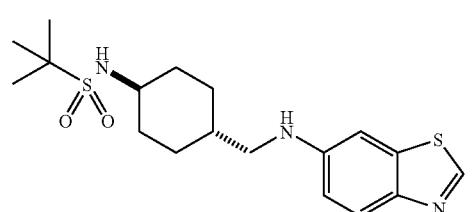
I-204



I-205

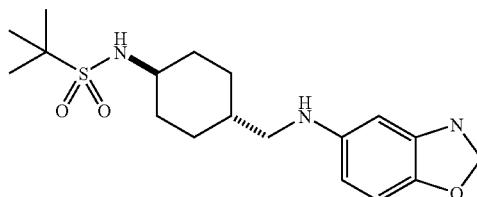


I-206

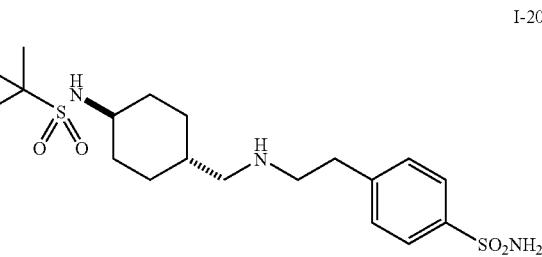


I-207

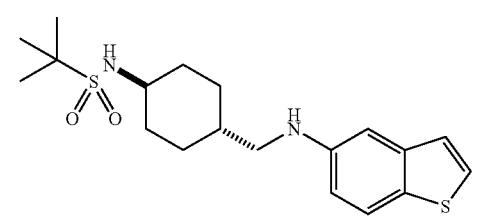
72
-continued



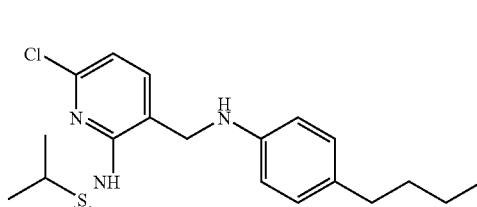
I-208



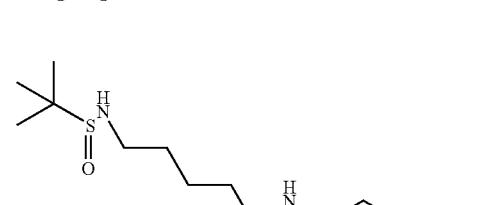
I-209



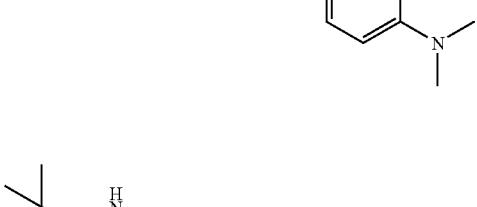
I-210



I-211



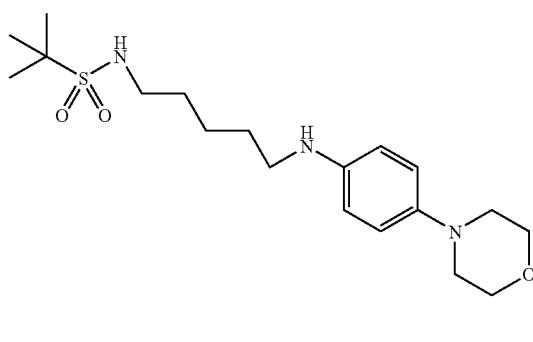
I-212



I-213

73
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I-214



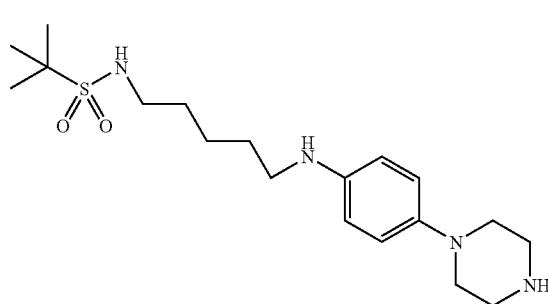
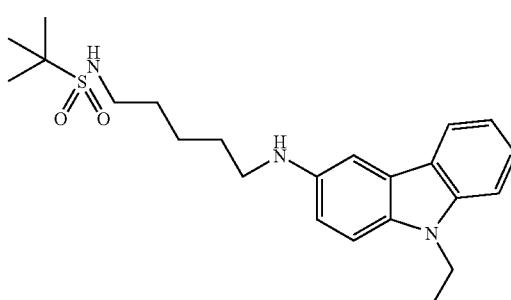
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74
-continued

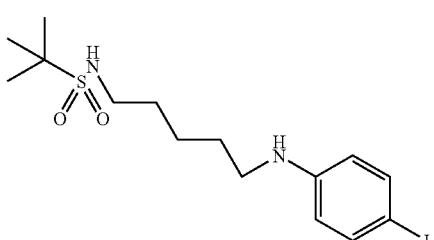
I-219



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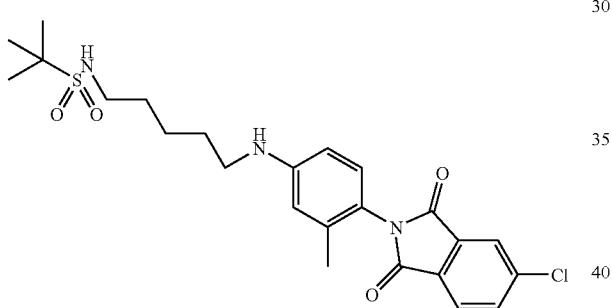
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I-220



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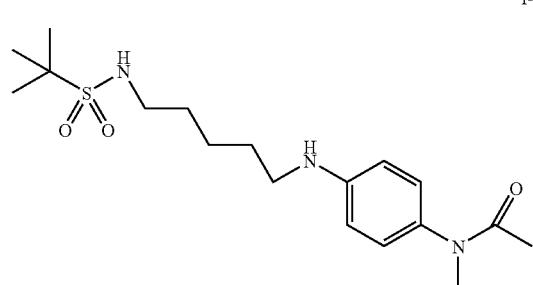
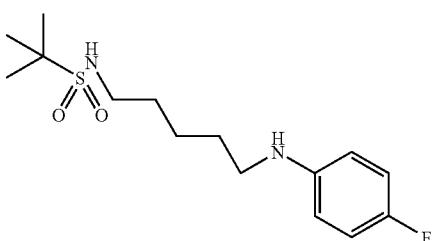
[Formula 80]



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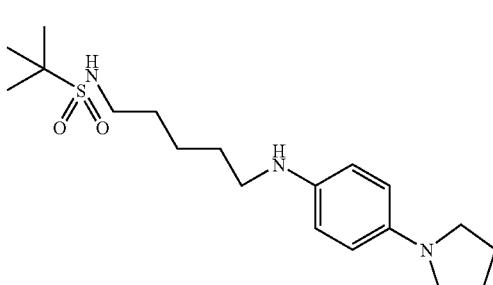
I-227



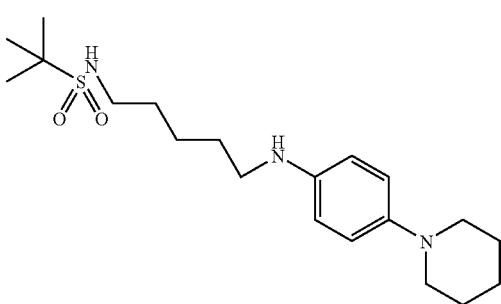
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I-228



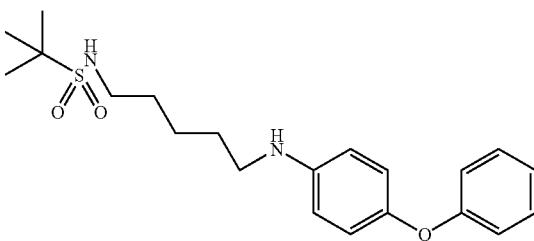
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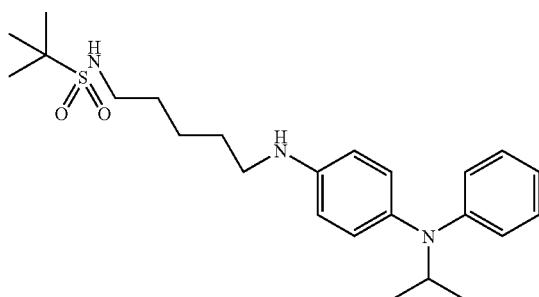
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I-229

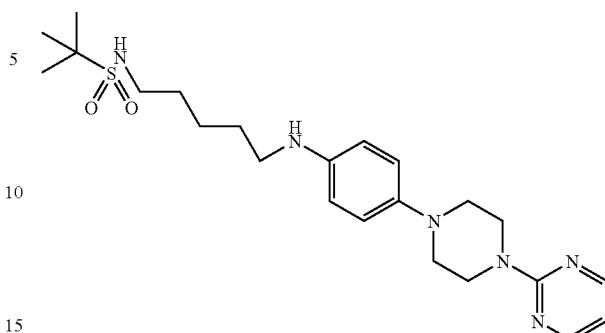


75
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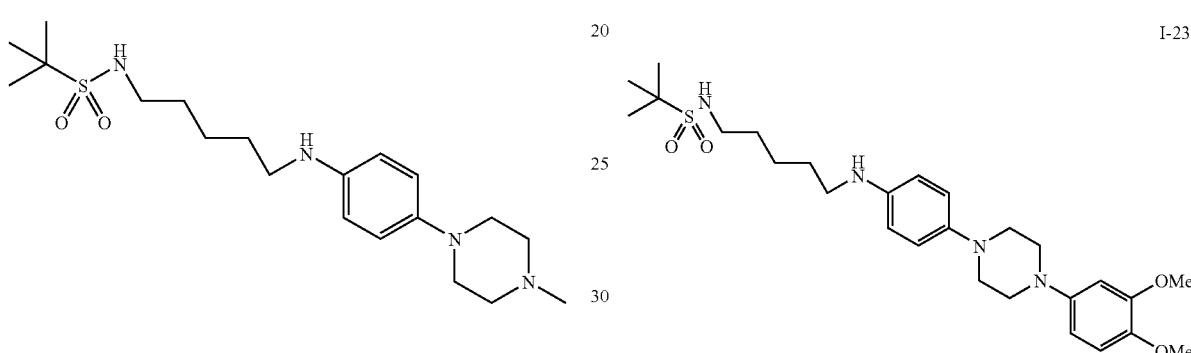
I-230

76
-continued



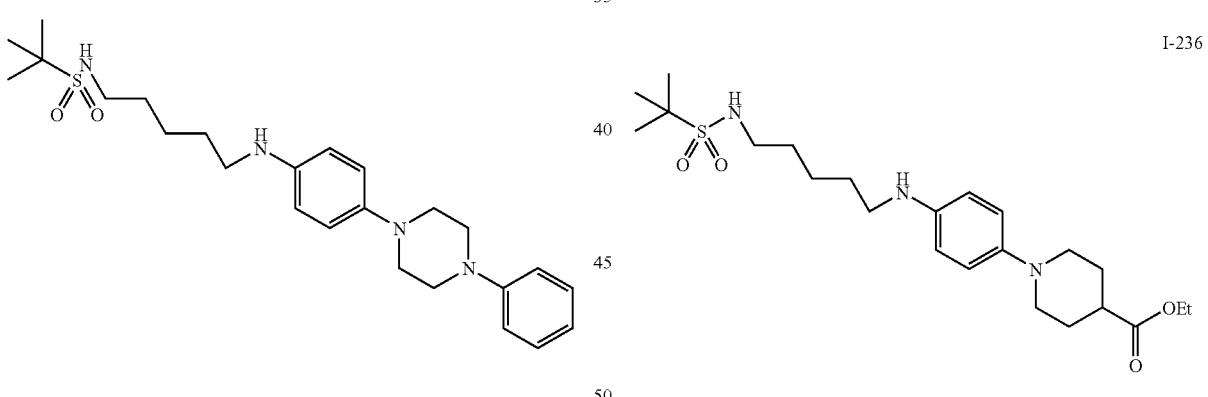
I-234

I-231



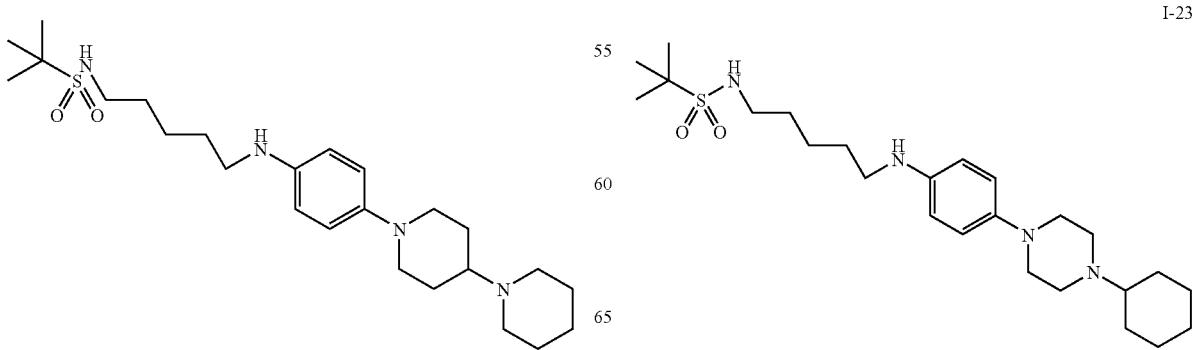
L-235

I-232 35



I-236

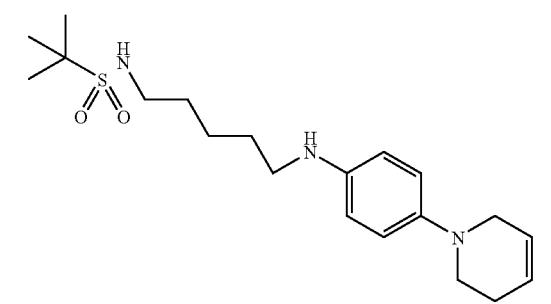
I-233



I-237

77
-continued

[Formula 81]



I-238

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I-239

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I-240

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I-241

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I-242

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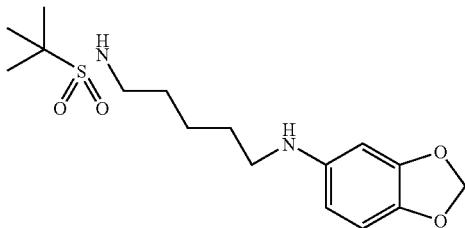
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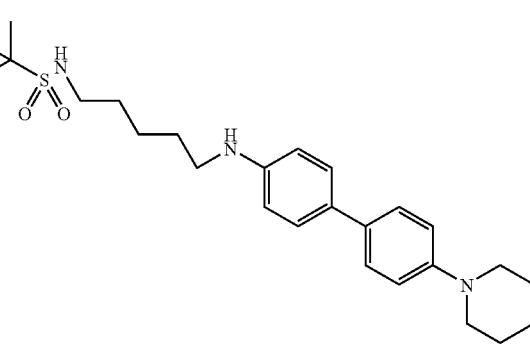
78
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I-243

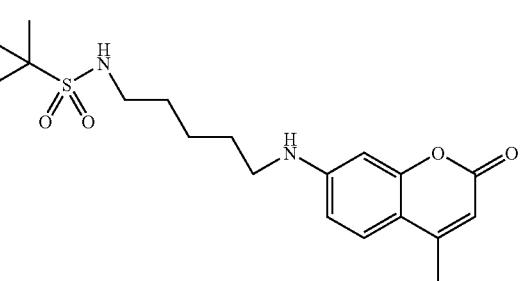


I-244

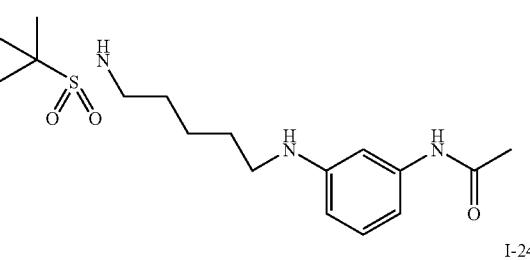
I-244



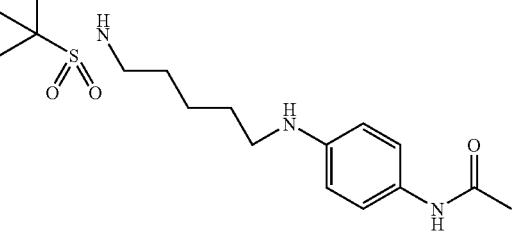
I-245



I-246



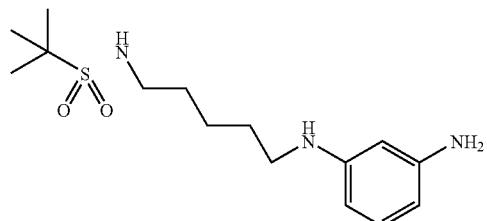
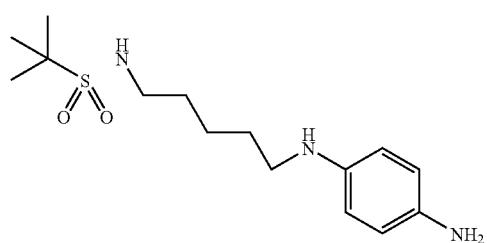
I-247



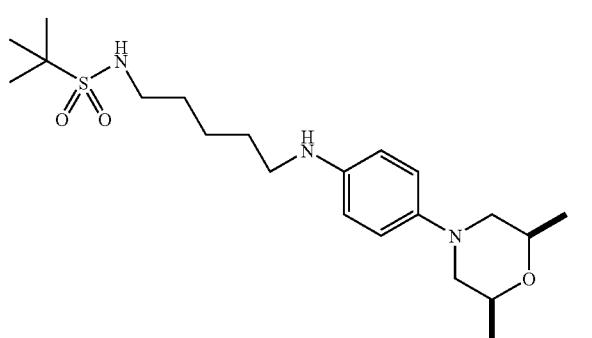
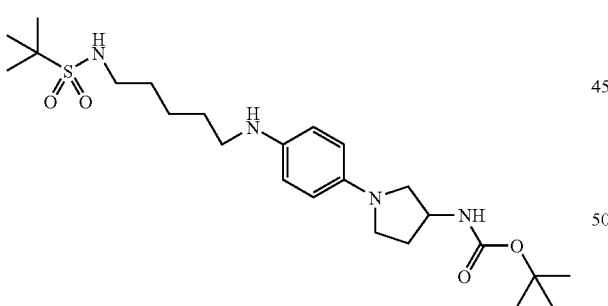
I-248

79
-continued

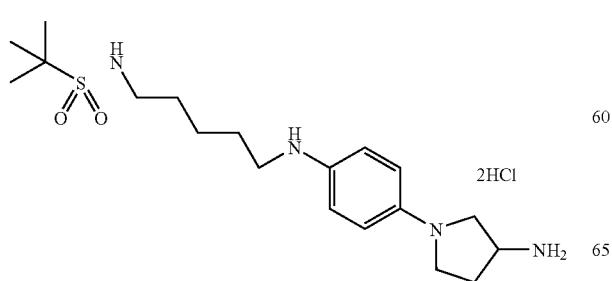
I-249

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I-250

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20I-251
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I-252

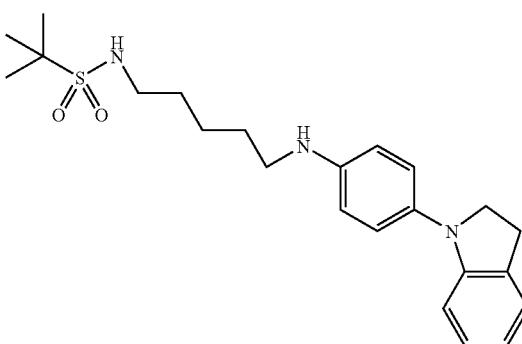
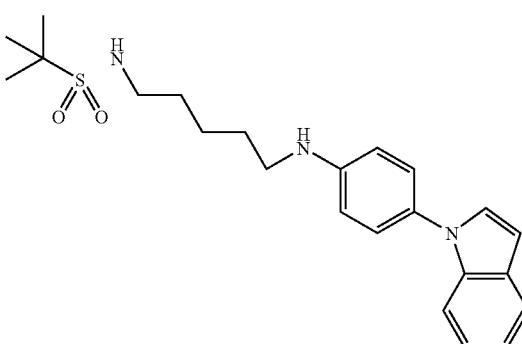
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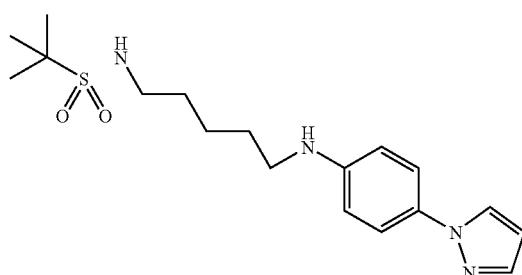
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80
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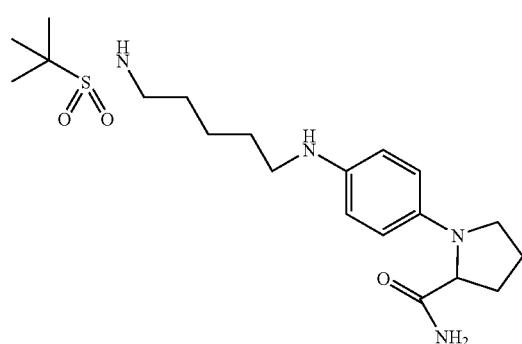
I-254

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I-25

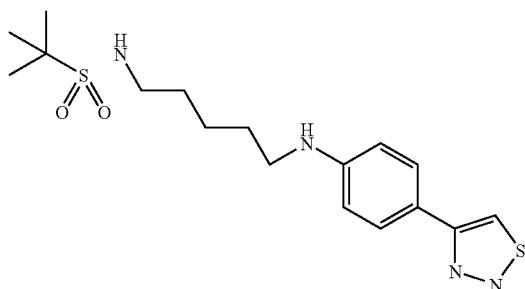


I-256



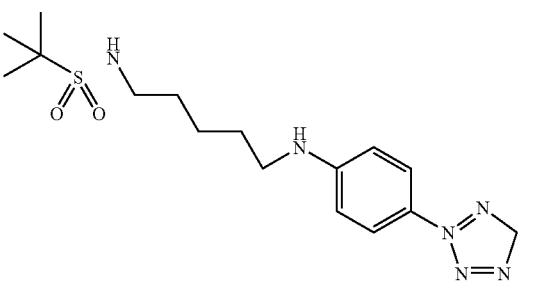
I-257

81
-continued

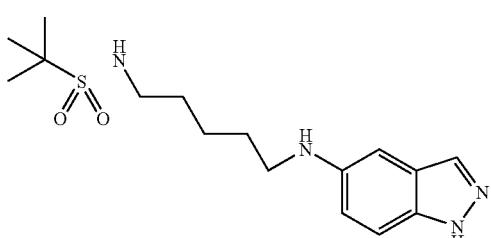


I-258

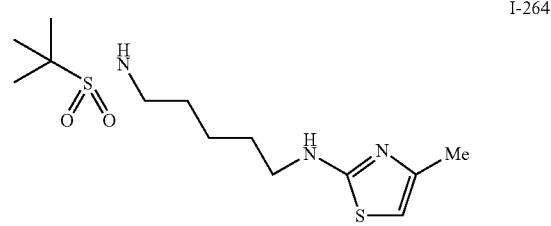
82



J-263

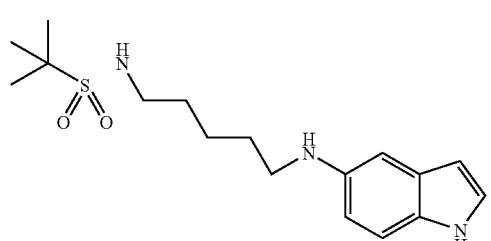


I-259

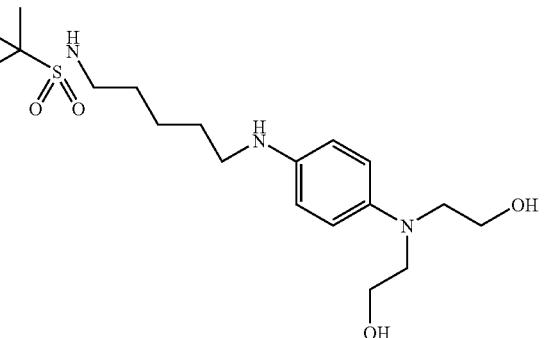


I-265

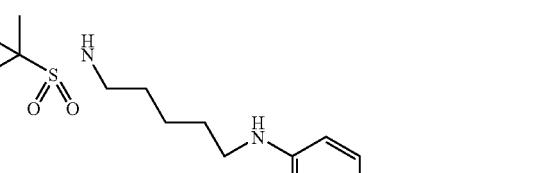
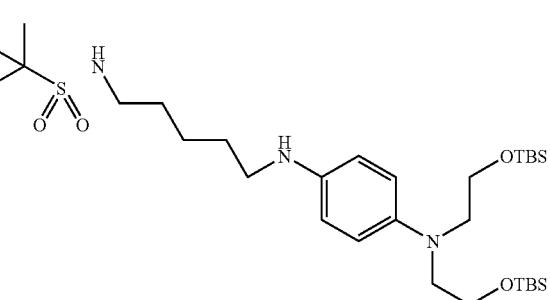
[Formula 82]



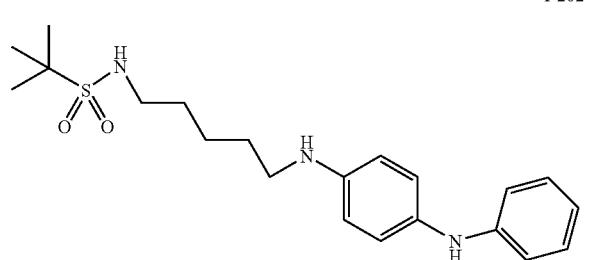
I-260



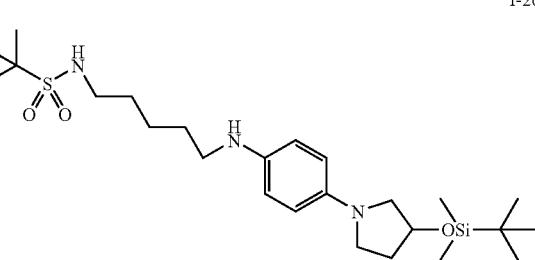
J-266



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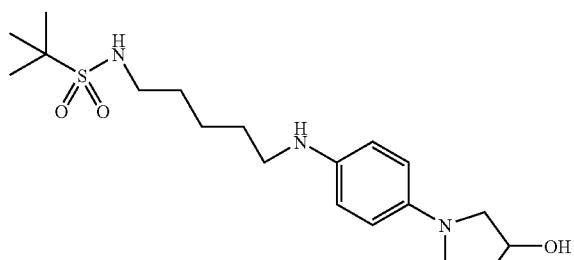
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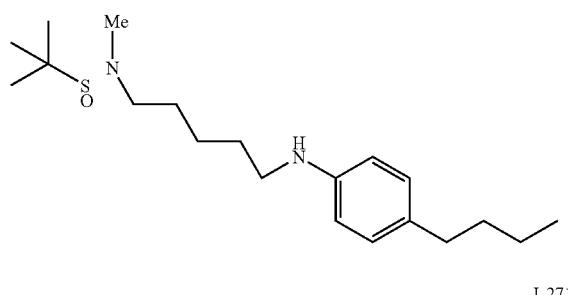
83

-continued

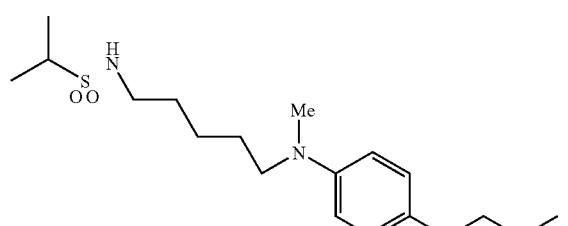
1-269



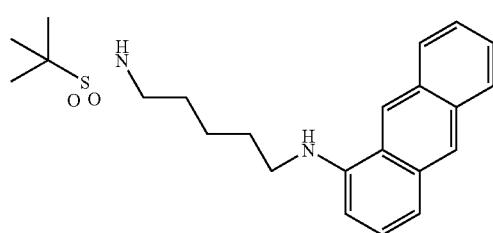
L-270 15



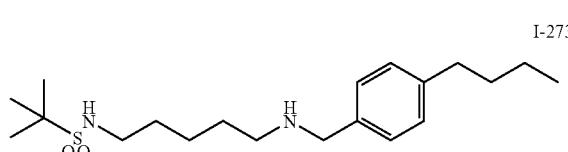
I-271



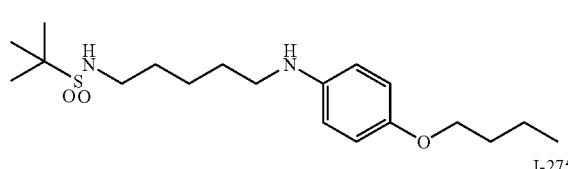
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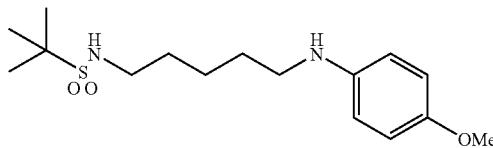
I-272



I-273



J 275

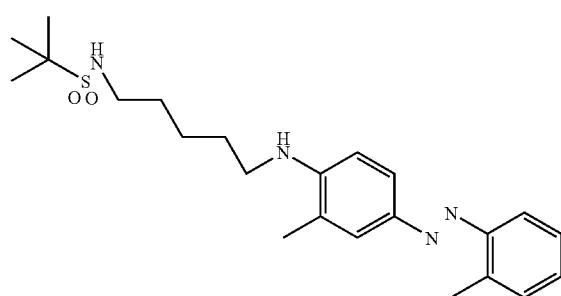


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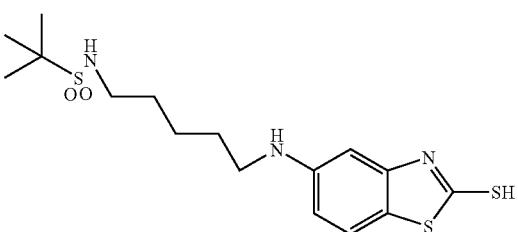
84

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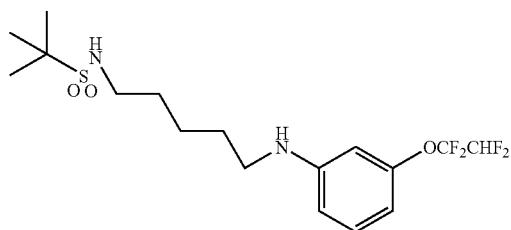
J-276



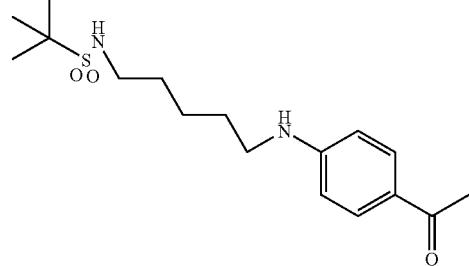
I-277



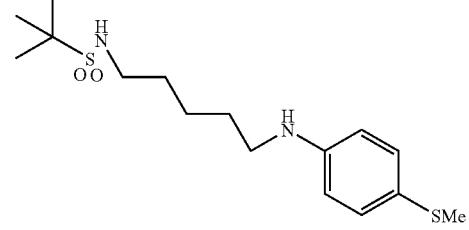
I-278



L-279



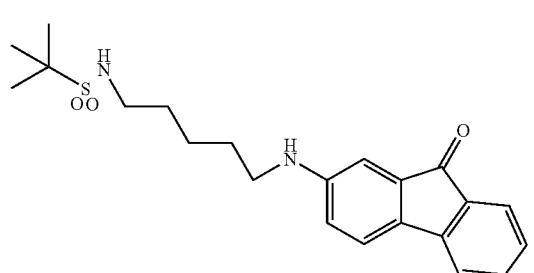
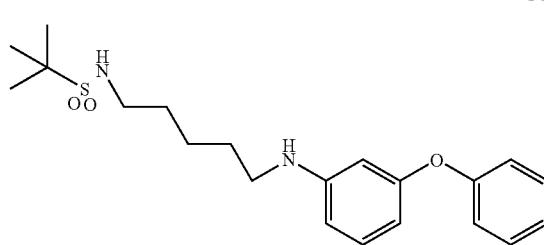
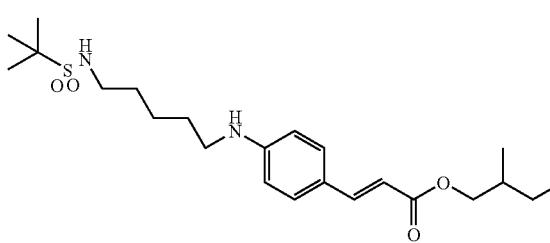
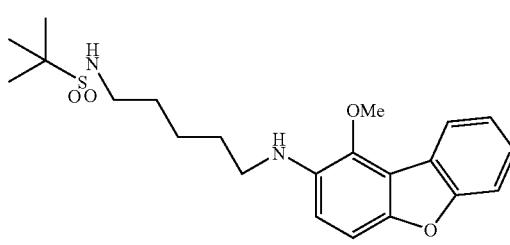
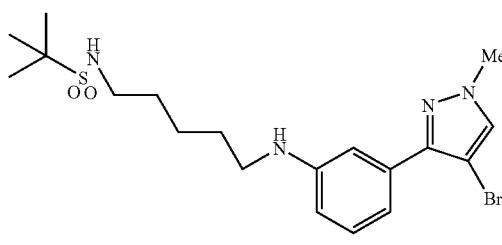
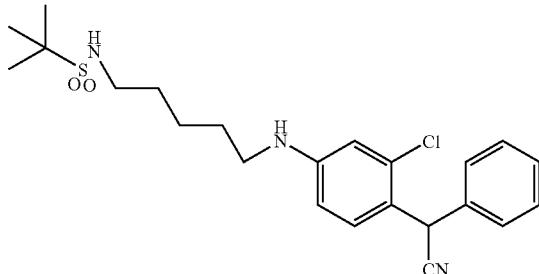
I-280



85

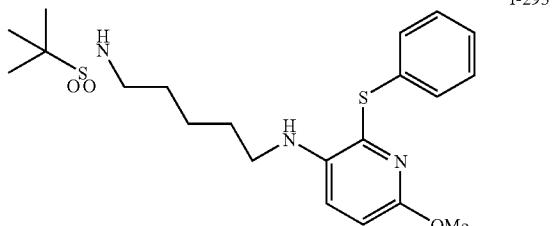
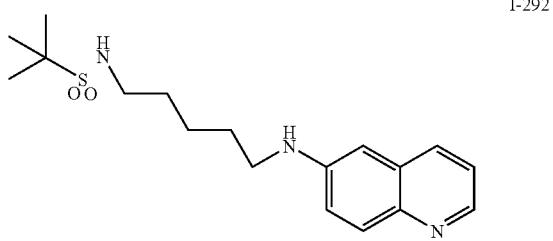
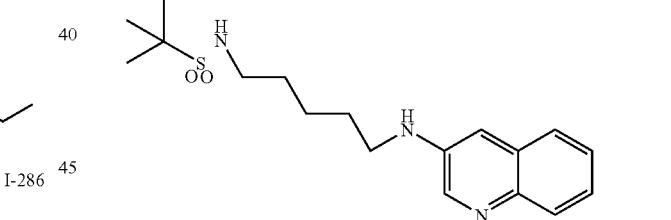
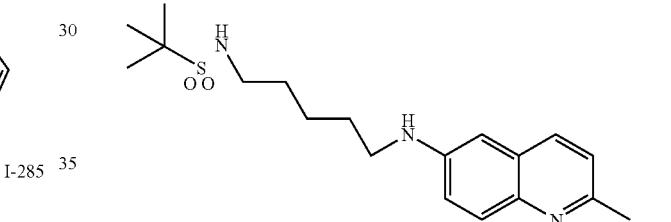
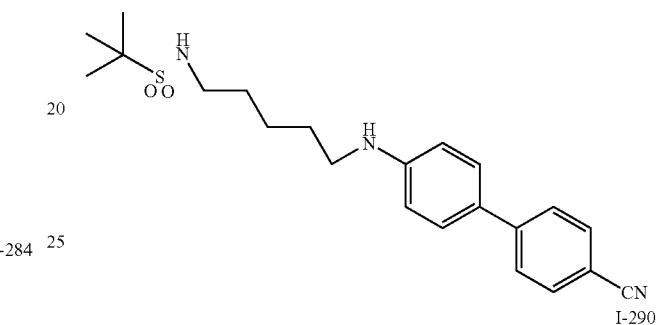
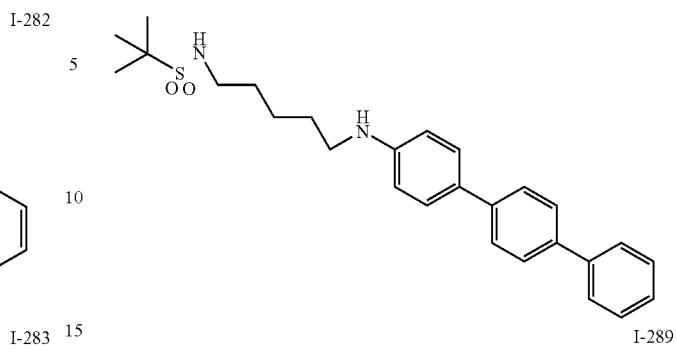
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[Formula 83]

**86**

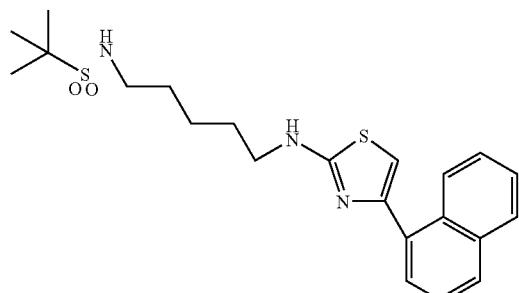
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I-288



87
-continued

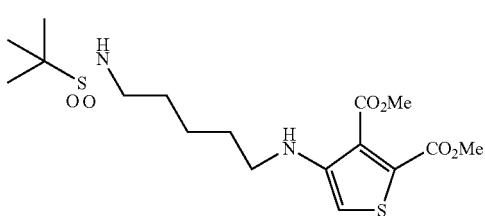
I-294



5

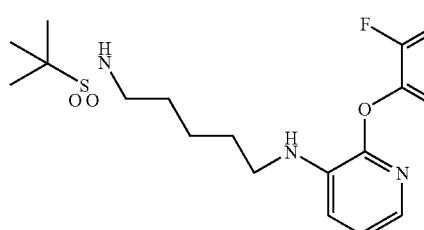
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I-295



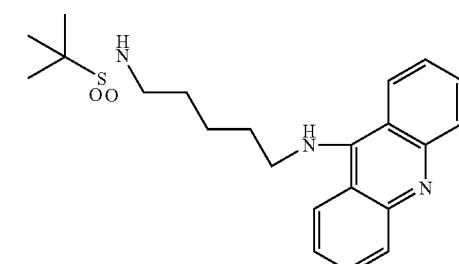
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I-296



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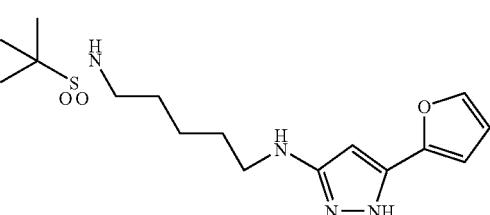
I-297



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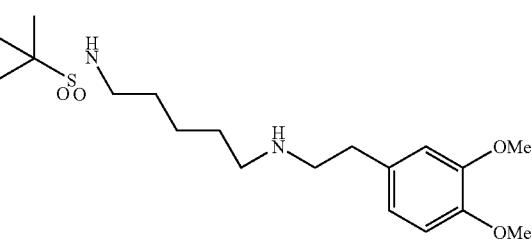
[Formula 84]

I-298



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I-299

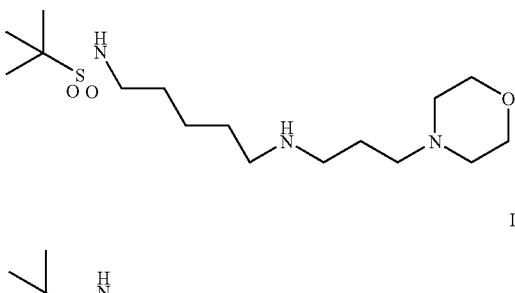


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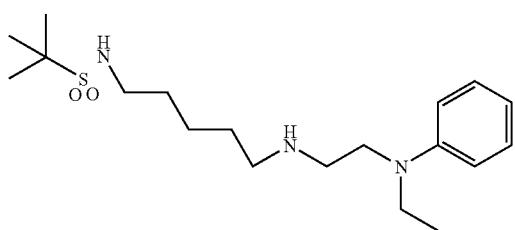
65

88
-continued

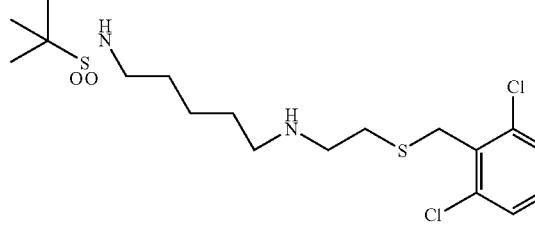
I-300



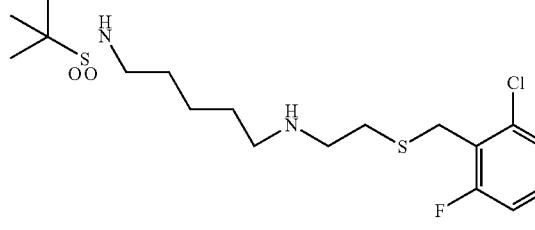
I-301



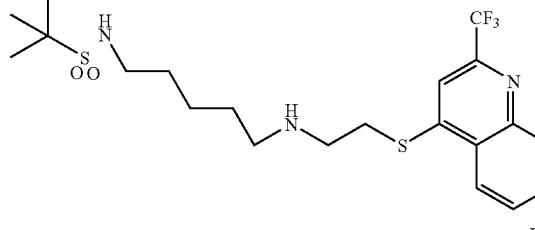
I-302



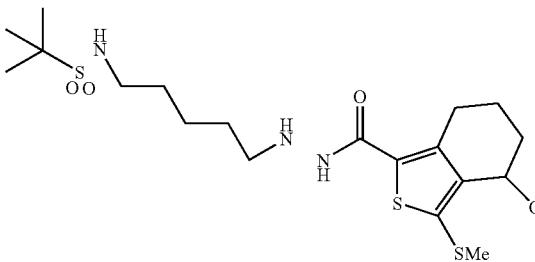
I-303



I-304

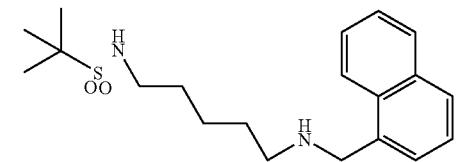


I-305



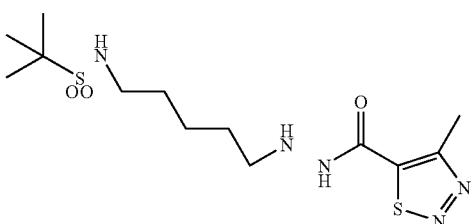
89
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I-306



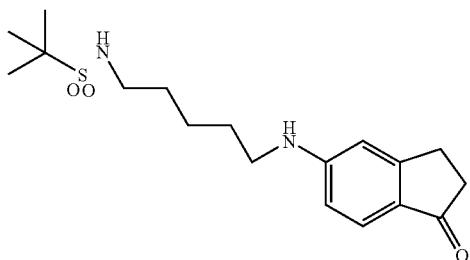
5

I-307 10



15

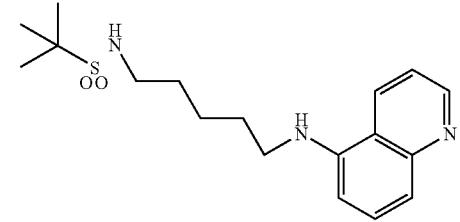
I-308



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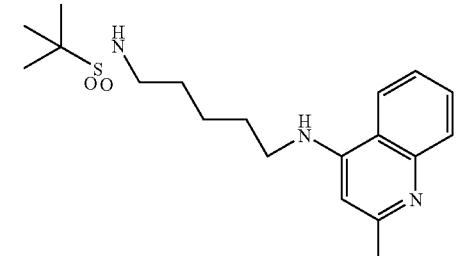
I-309

35



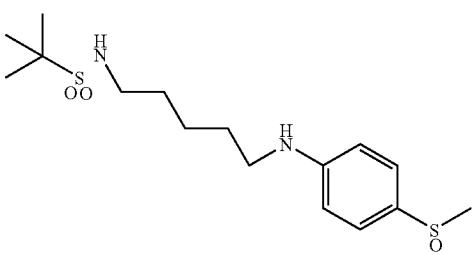
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I-310 45



55

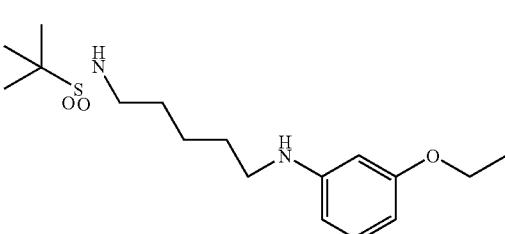
I-311



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90
-continued

I-312



I-313

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I-308

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I-314

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I-314

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I-314

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I-314

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I-315

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I-315

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I-316

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I-316

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I-317

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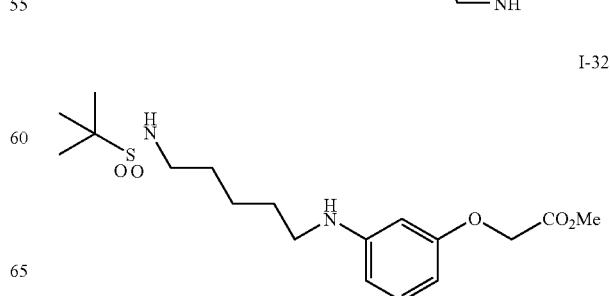
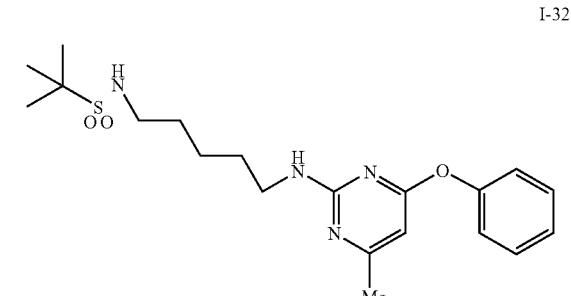
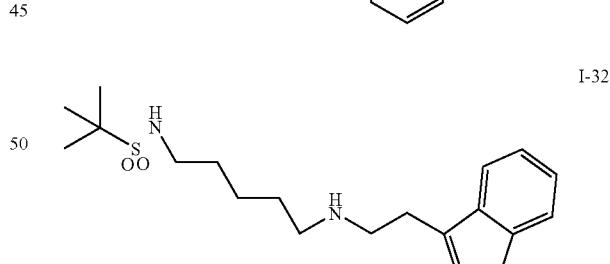
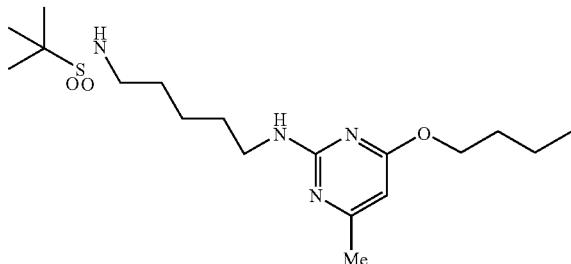
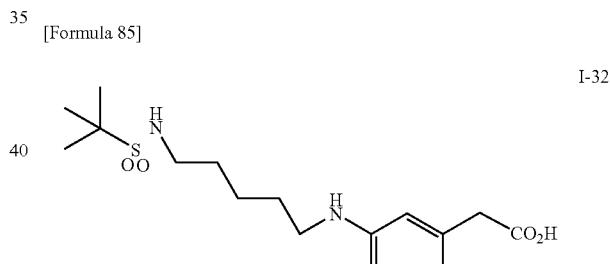
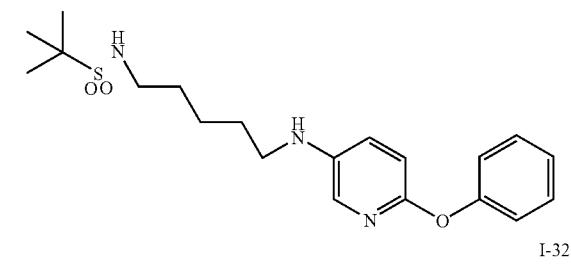
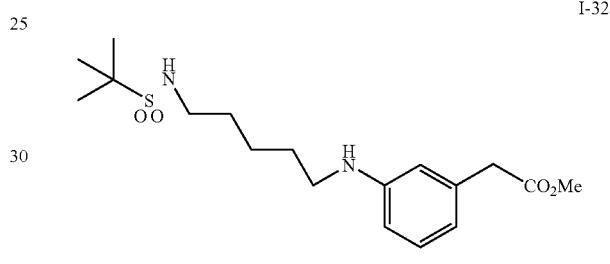
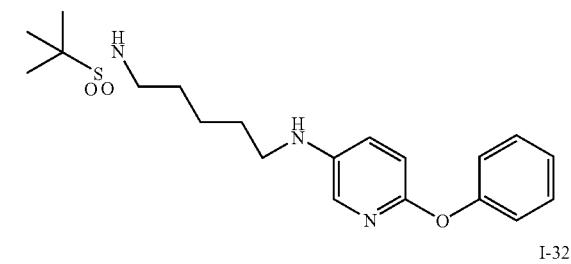
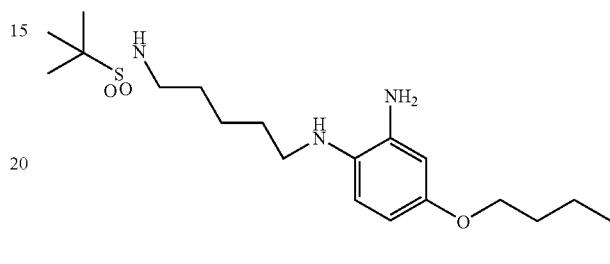
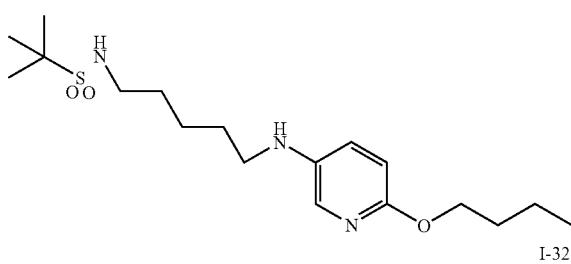
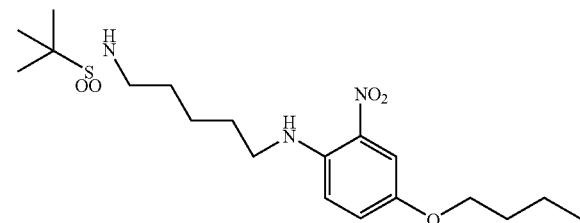
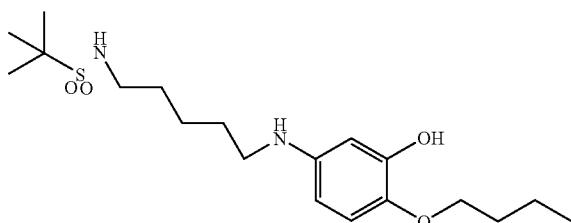
I-317

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I-317

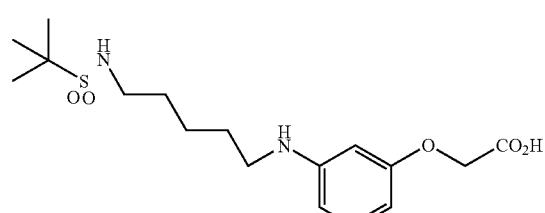
91
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I-318

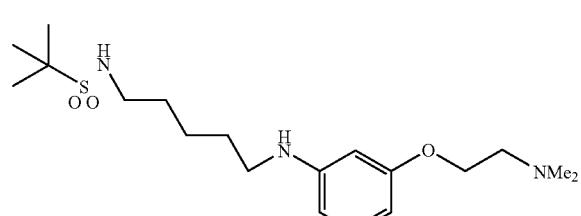


93
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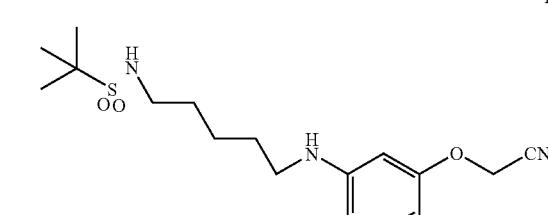
I-329



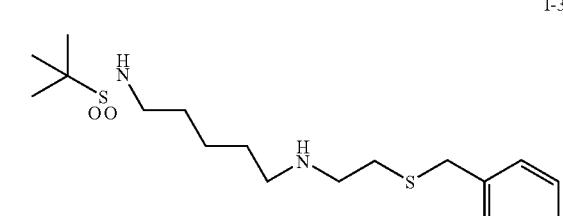
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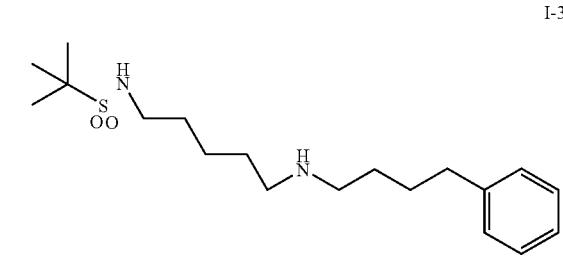
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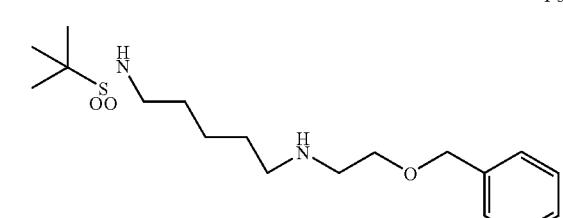
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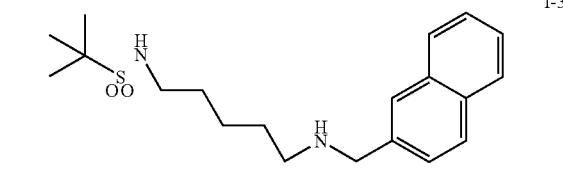
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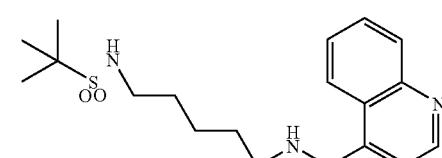
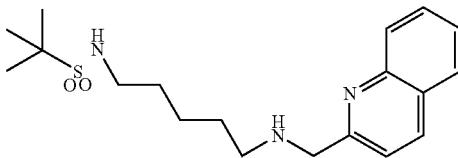
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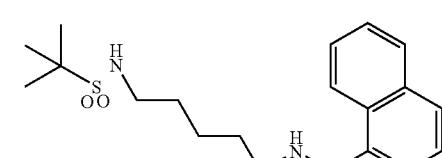
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94
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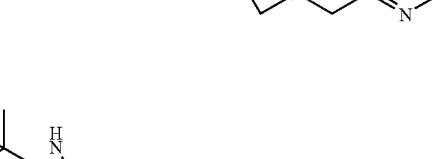
I-336



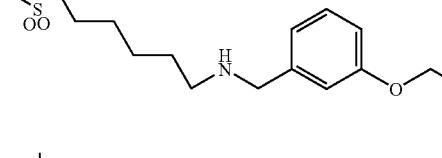
I-337



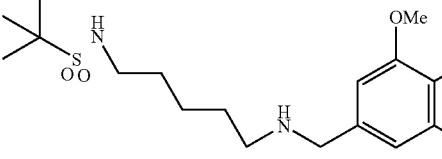
I-338



I-339



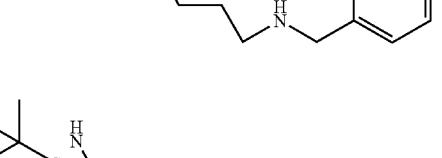
I-340



I-341



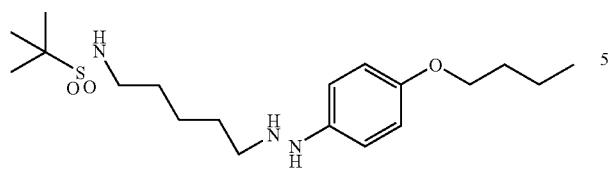
I-342



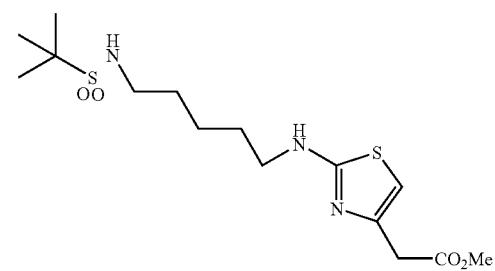
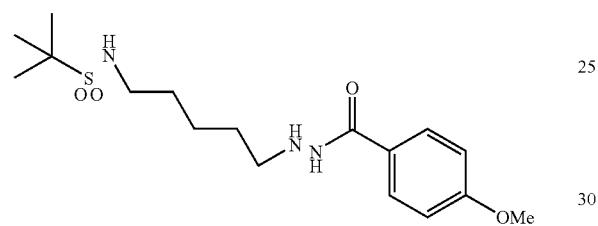
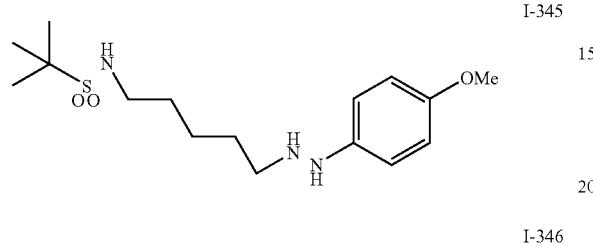
I-343

95
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I-344

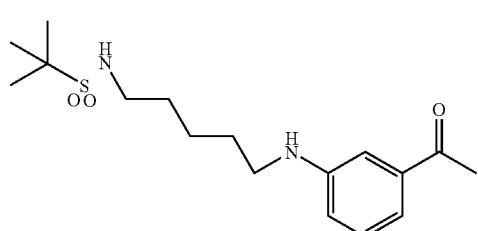
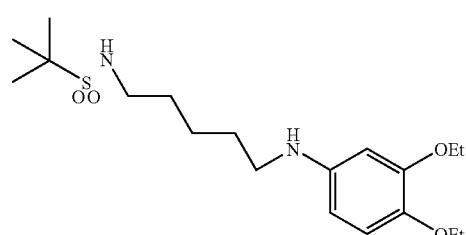


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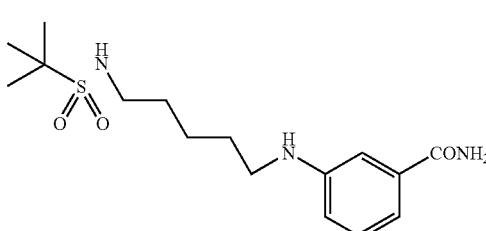
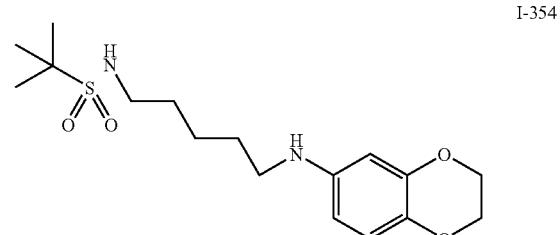
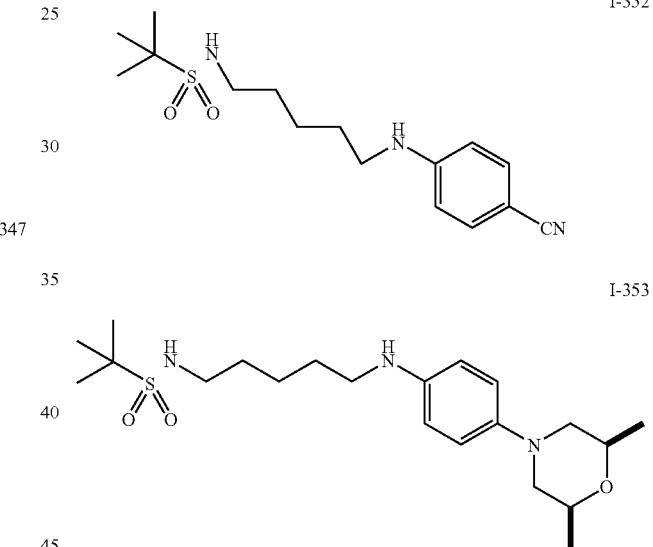
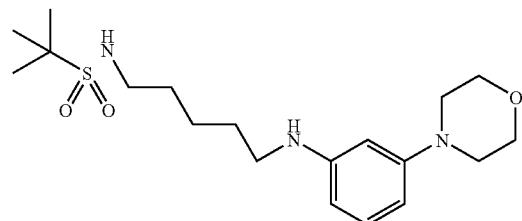
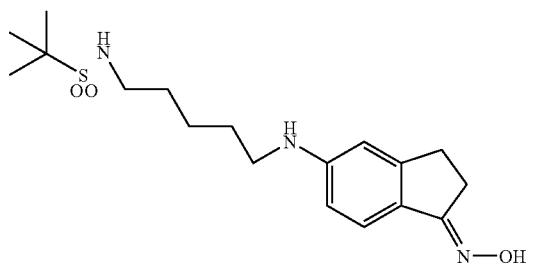
[Formula 86]

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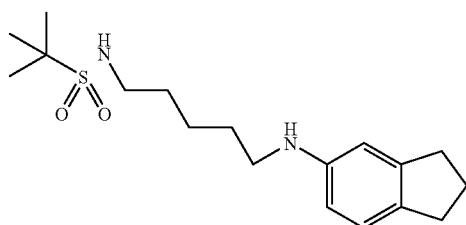


96
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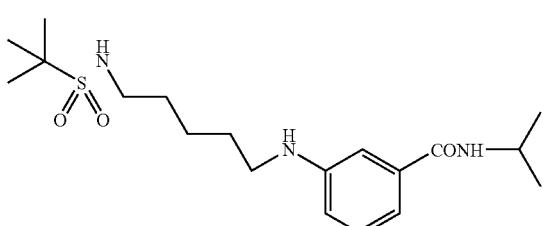
I-350



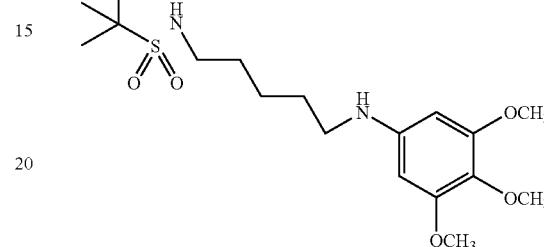
97
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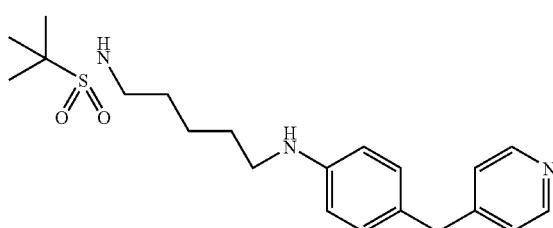
I-356



I-357



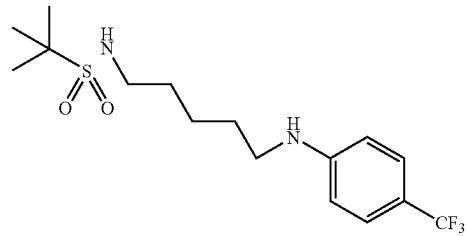
I-358



I-359

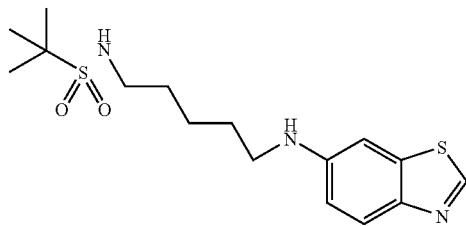
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I-360 40 [Formula 87]
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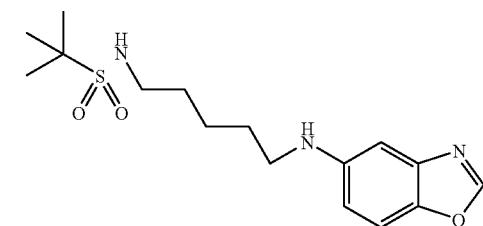


I-364

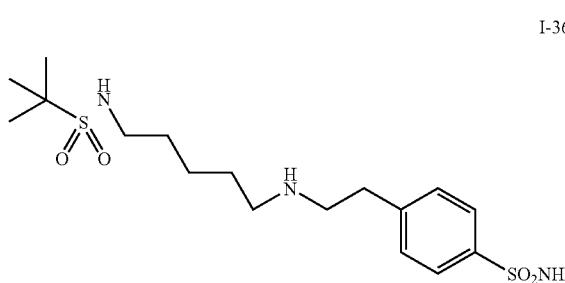
I-365



I-366



I-367



I-361

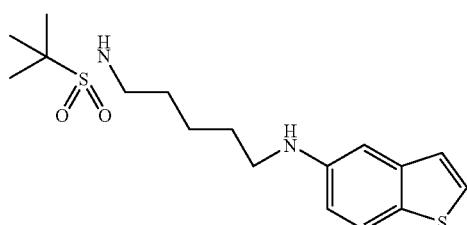
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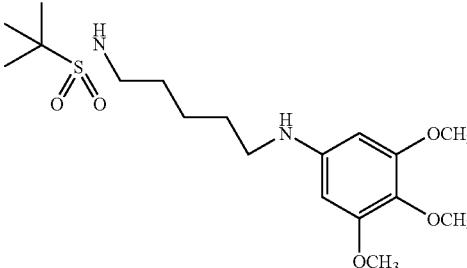
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98
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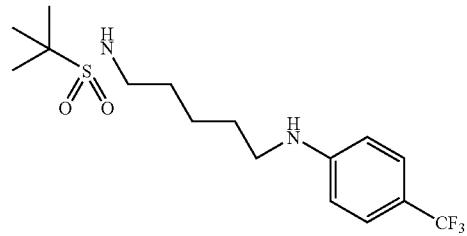
I-362



I-363



I-364



I-365

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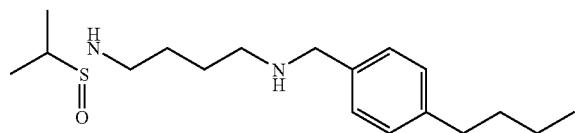
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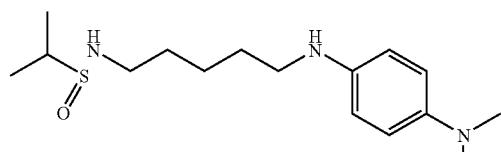
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99
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I-369

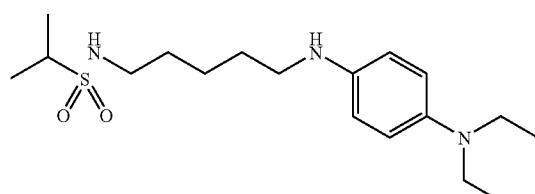


I-370 10

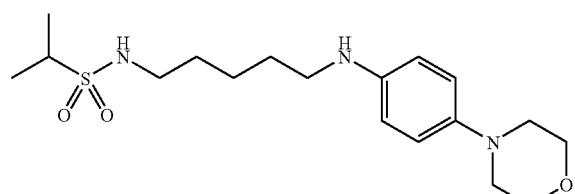


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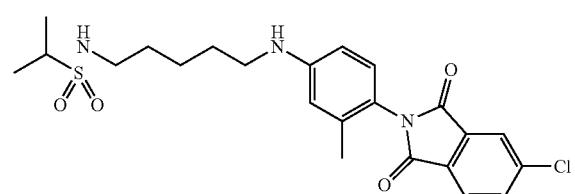
I-371 20



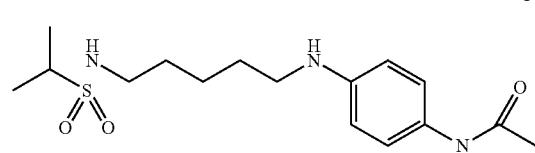
I-372 30



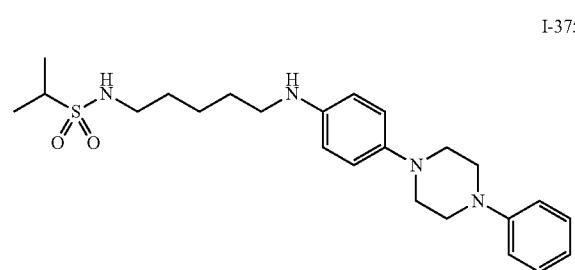
I-373 40



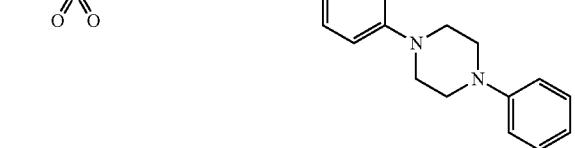
I-374 45



I-375 50



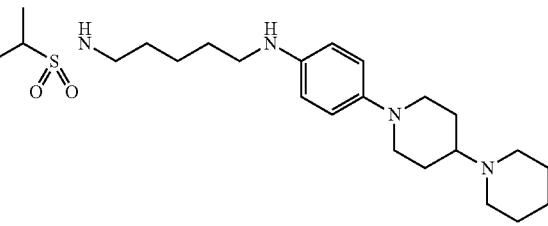
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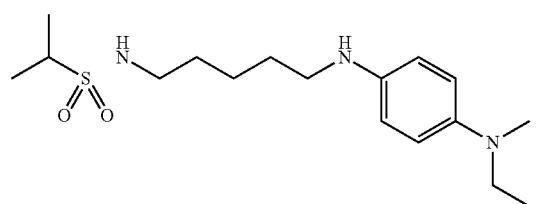
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100
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I-376

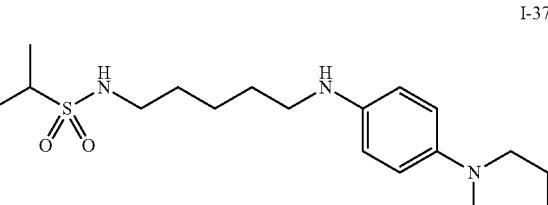


I-377

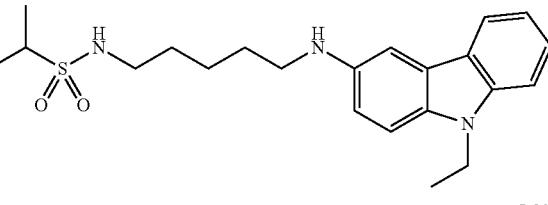


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I-371 20

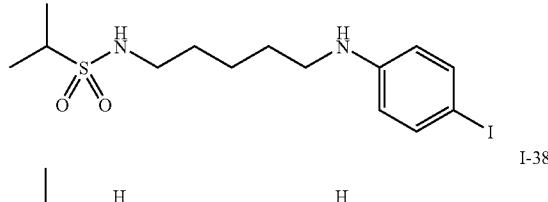


I-372 30

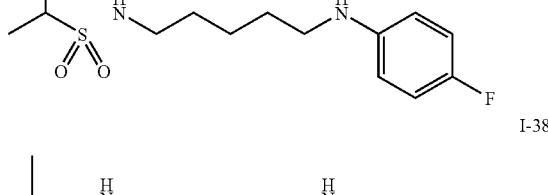


I-379

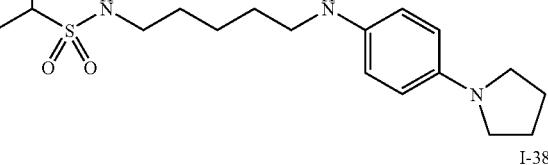
I-373 40



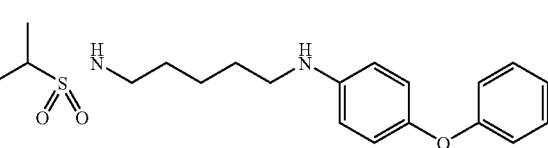
I-380



I-381



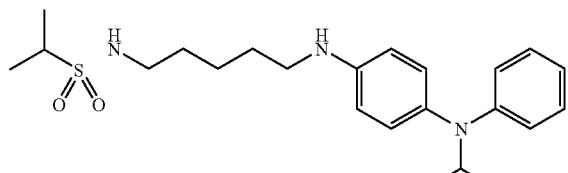
I-382



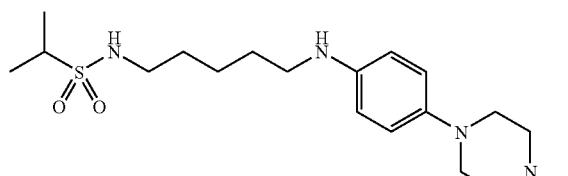
I-383

101

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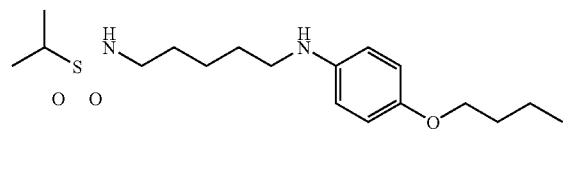


I-385



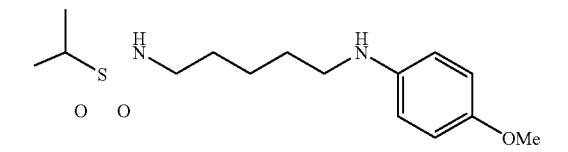
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I-386



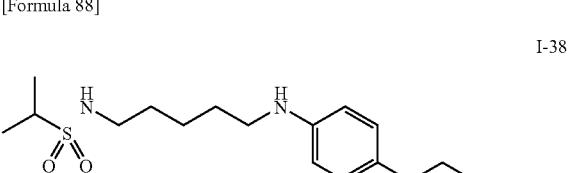
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I-387



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I-388

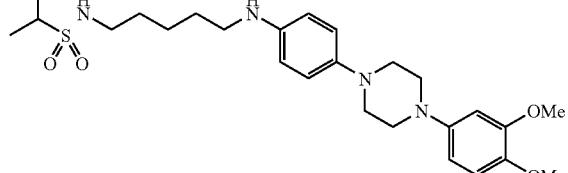


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I-389

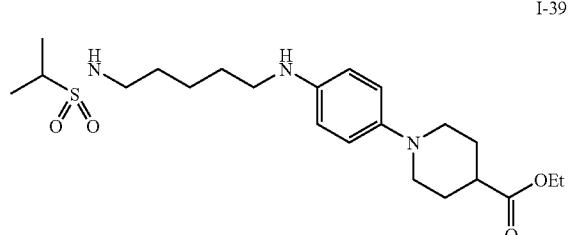


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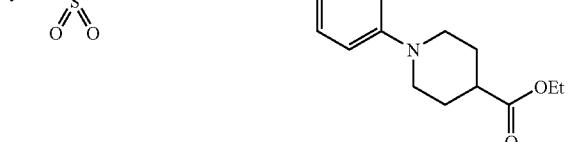
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I-391



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I-392



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I-393



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I-394



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I-395



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I-396



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I-397



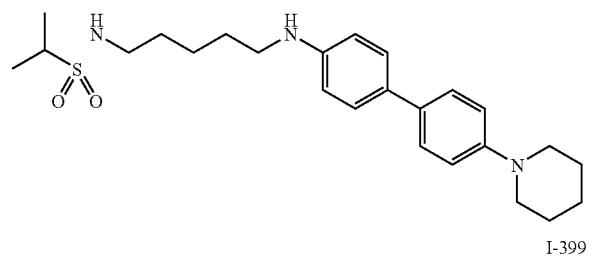
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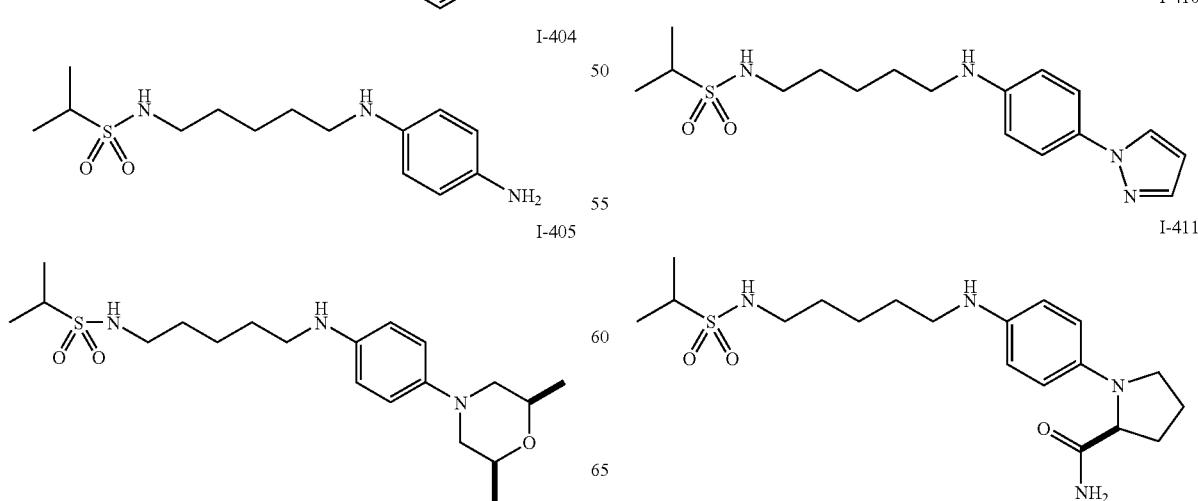
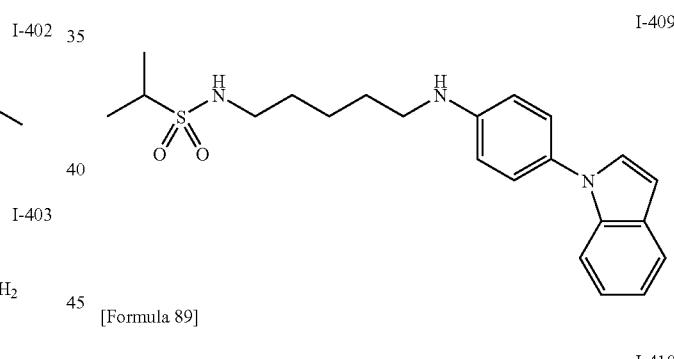
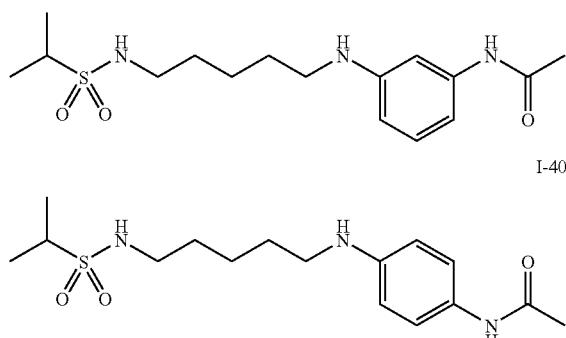
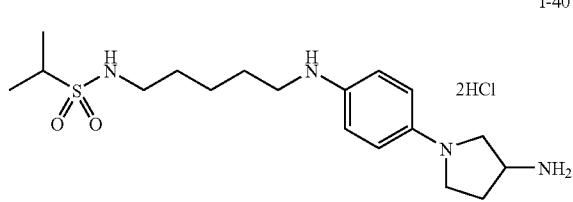
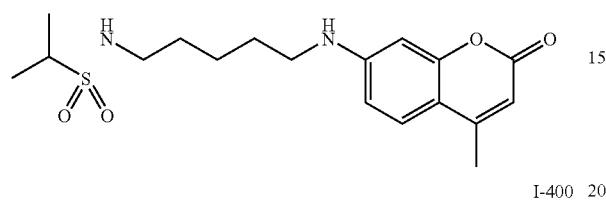
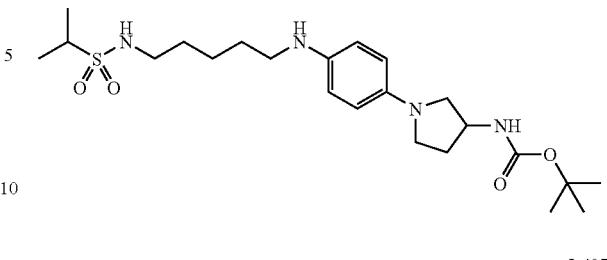
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103

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**104**

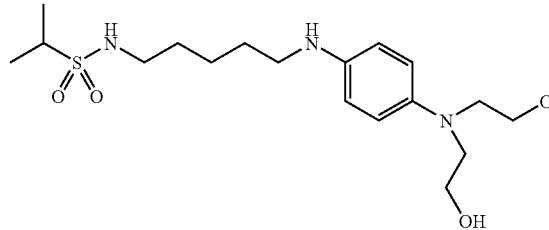
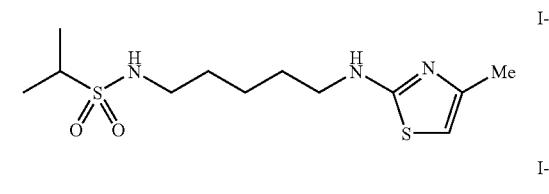
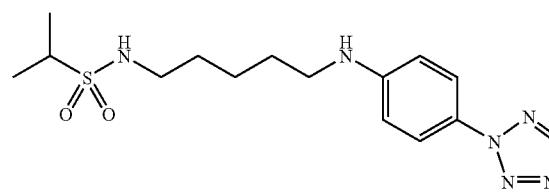
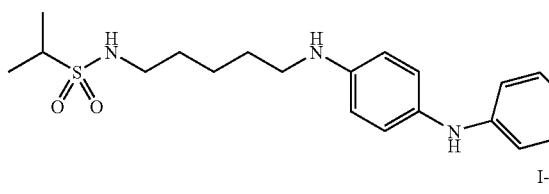
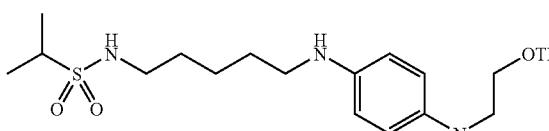
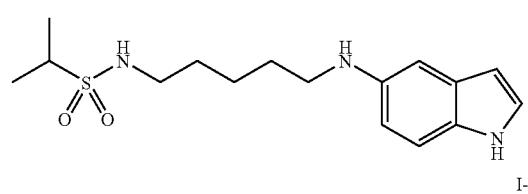
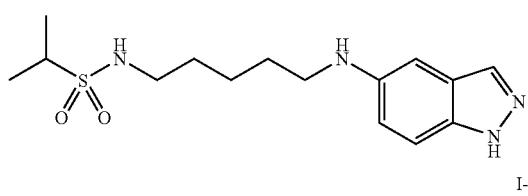
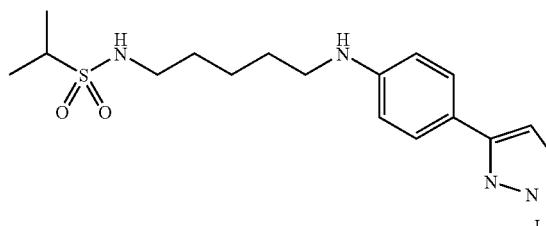
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105

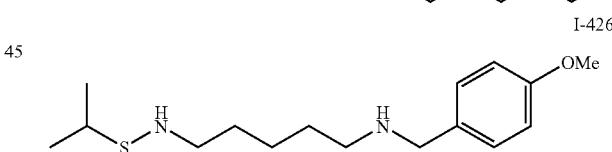
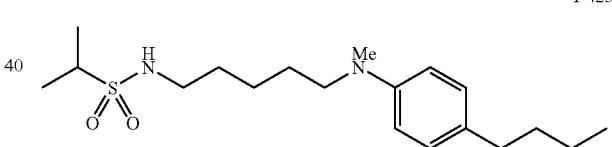
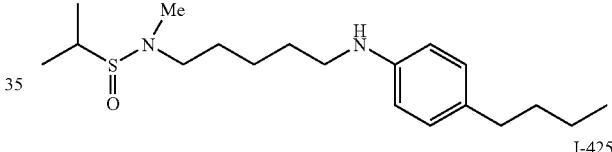
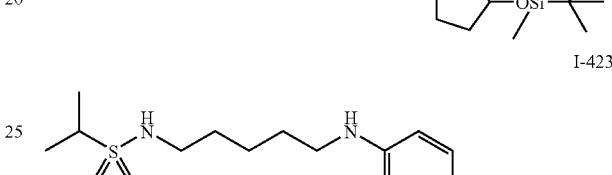
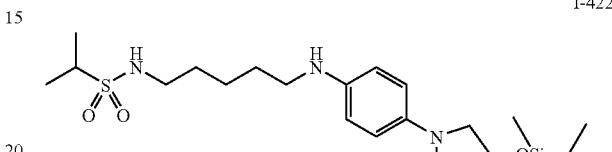
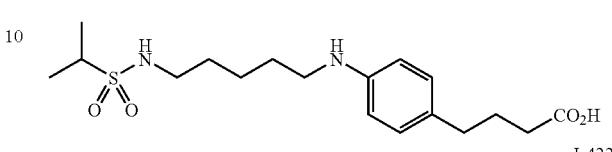
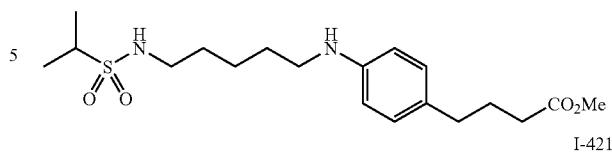
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I-412

**106**

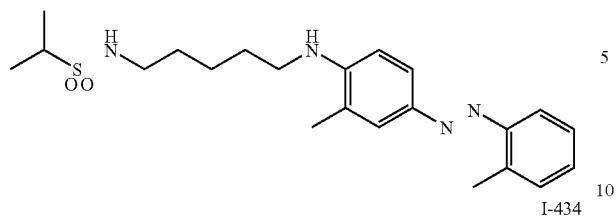
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I-420



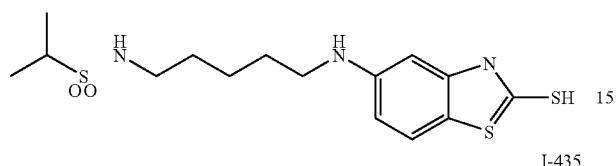
107
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I-433

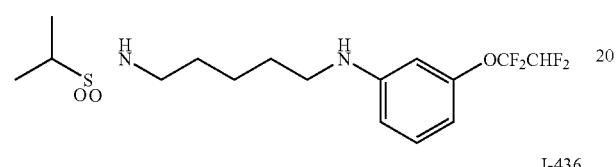


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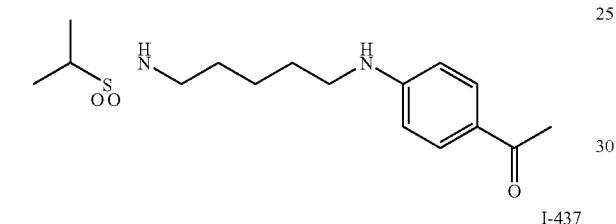


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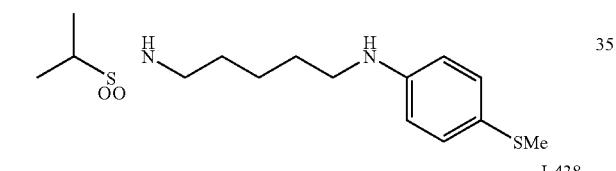


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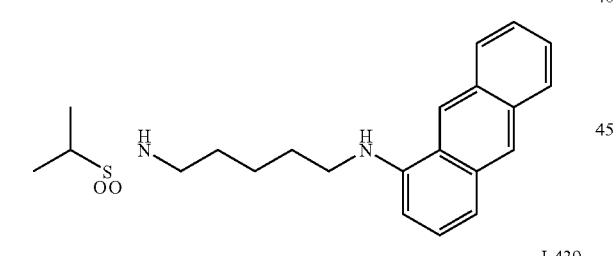


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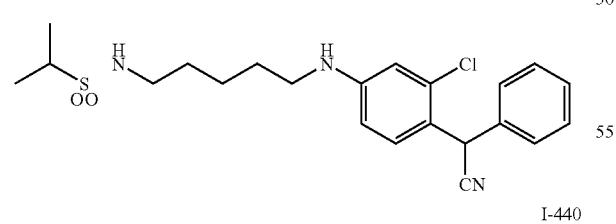
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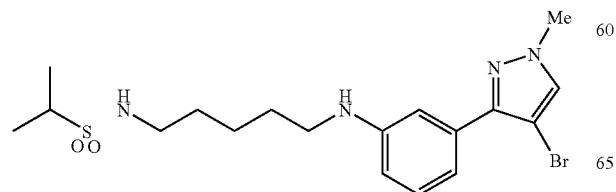
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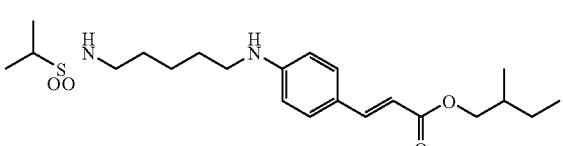
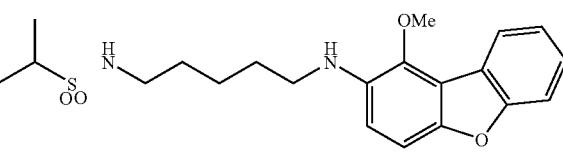
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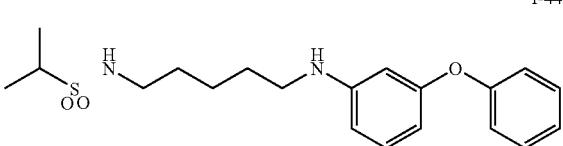
108
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I-442

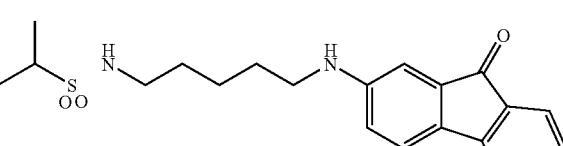
I-441



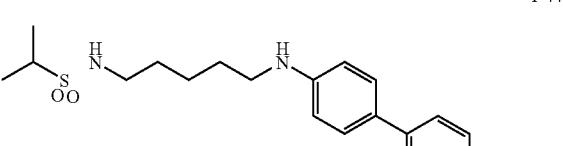
I-443



I-444



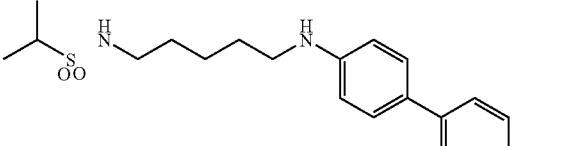
I-445



I-446



I-447



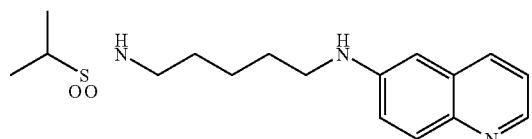
I-448

109

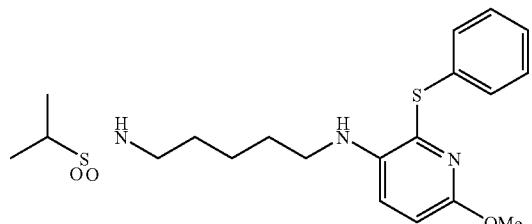
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I-449

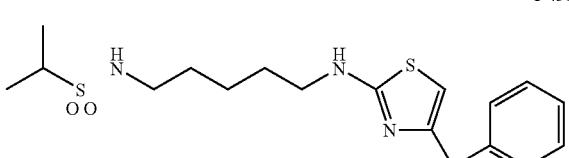
[Formula 91]



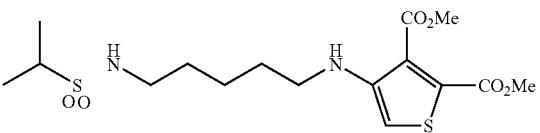
I-450 10



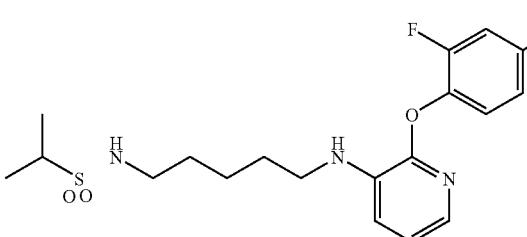
I-451



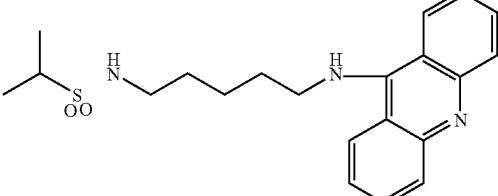
I-452



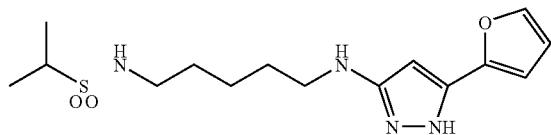
I-453 40



I-454



I-455 60



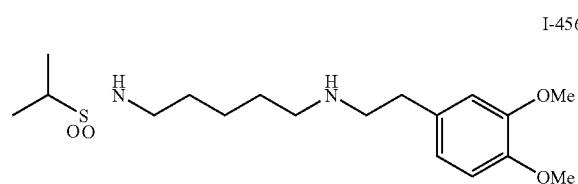
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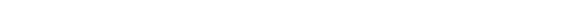
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I-456

I-456



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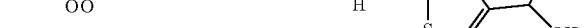
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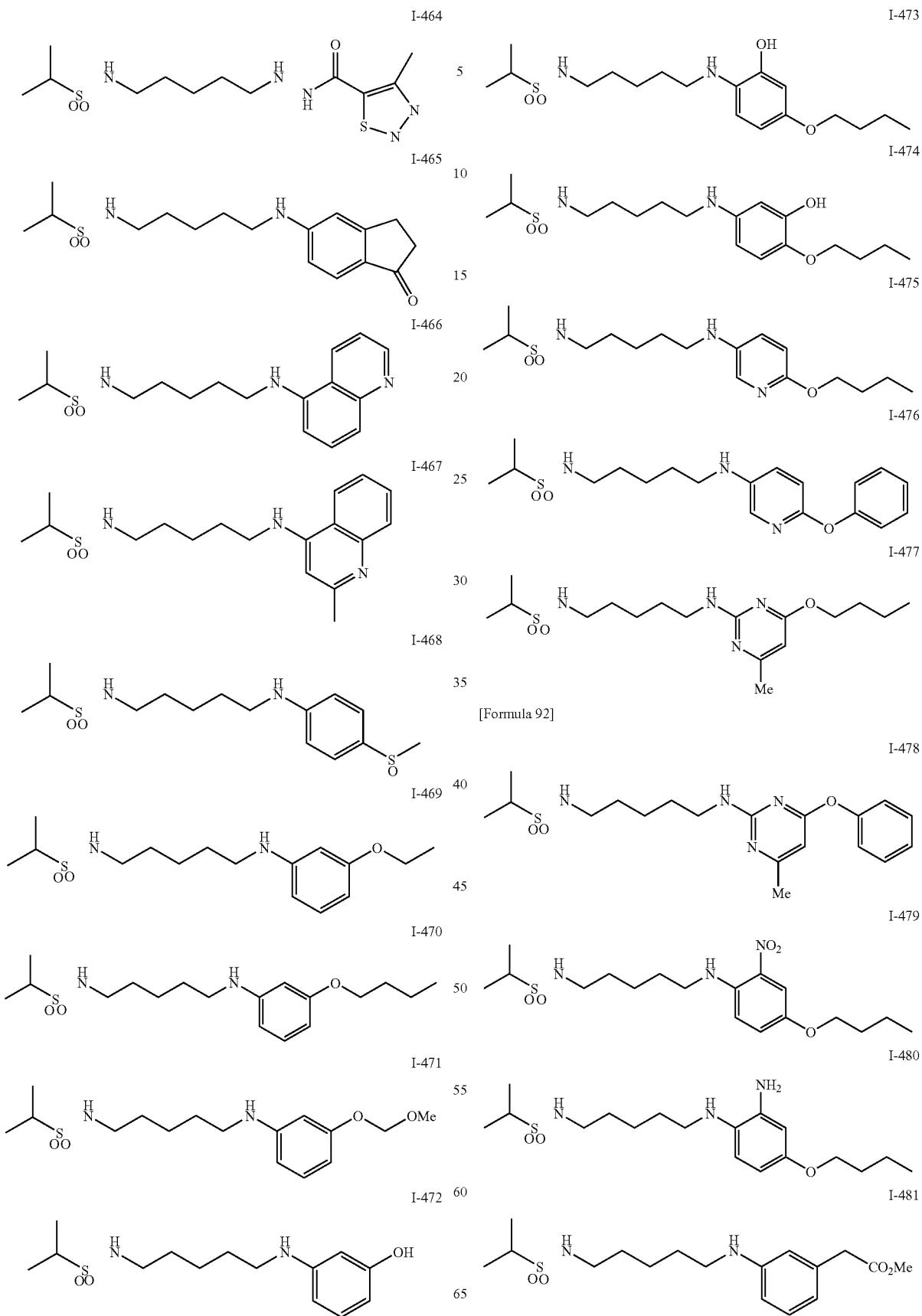


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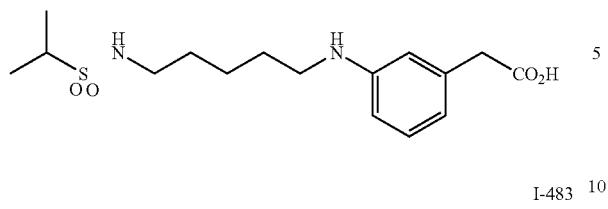
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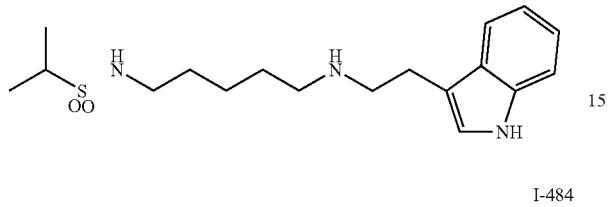
111
-continued**112**
-continued

113
-continued

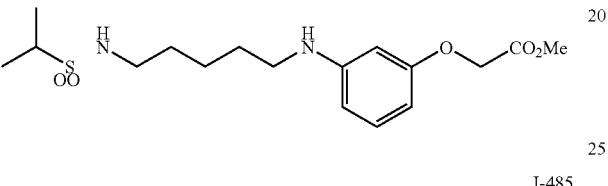
I-482



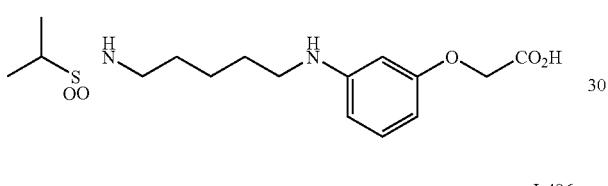
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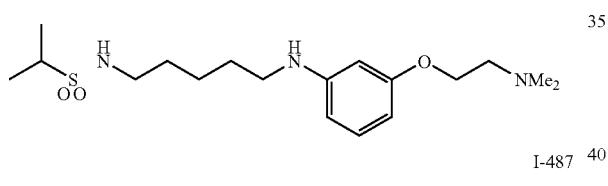
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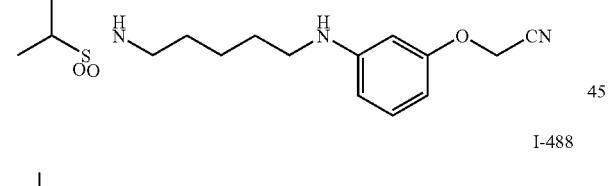
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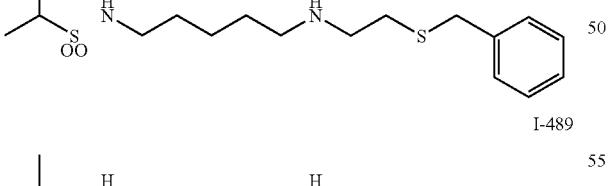
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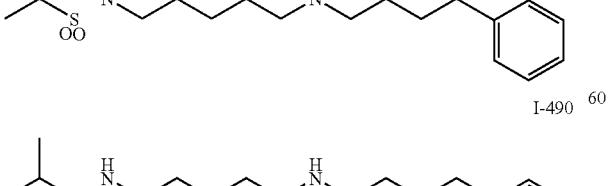
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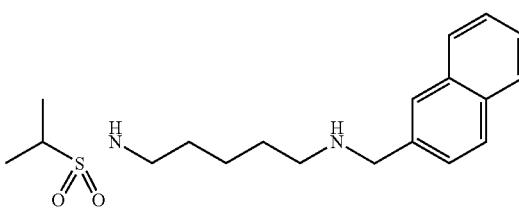
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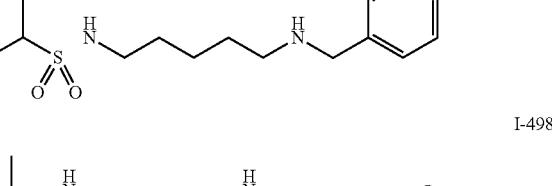
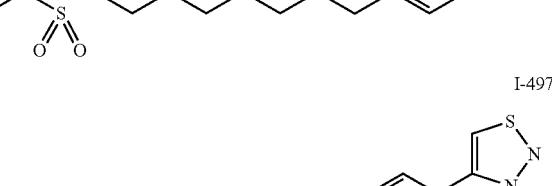
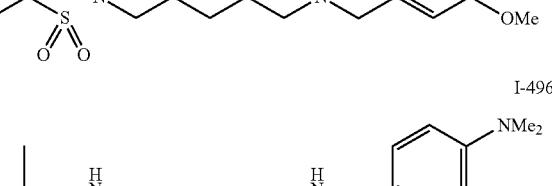
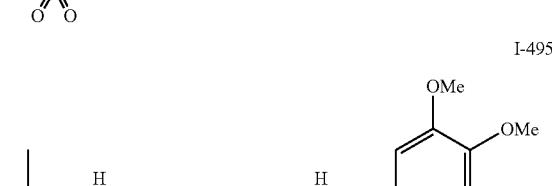
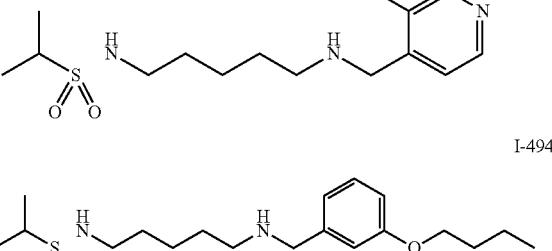
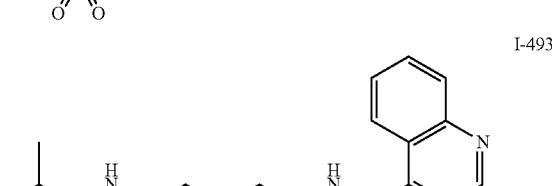
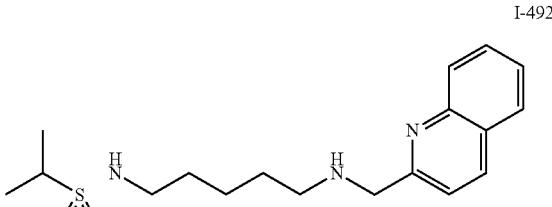
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114
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I-491



I-491



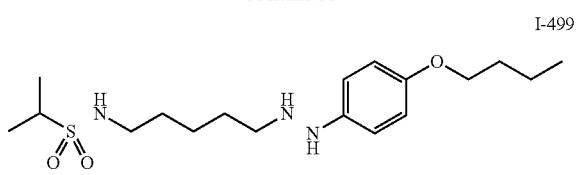
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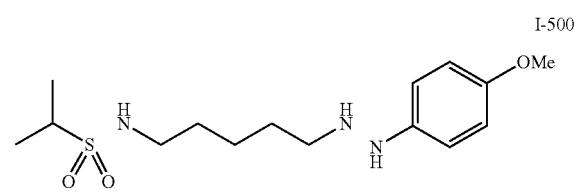
115

-continued

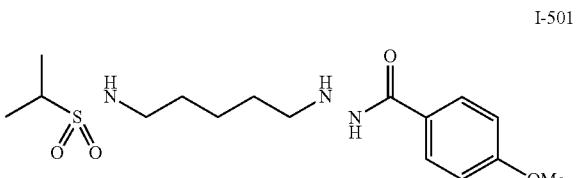


[Formula 93]

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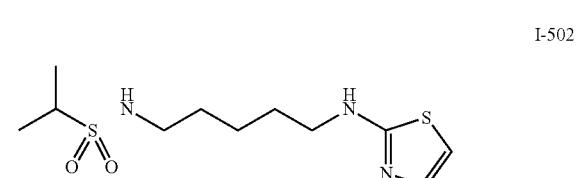


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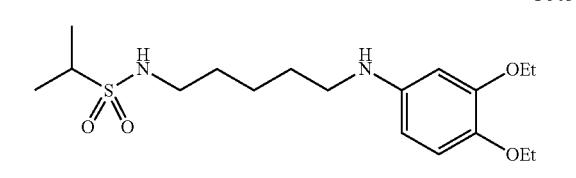
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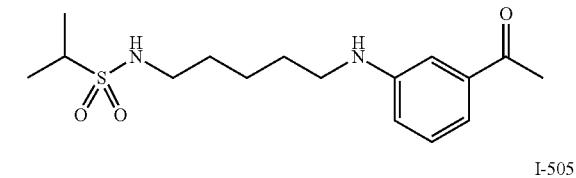
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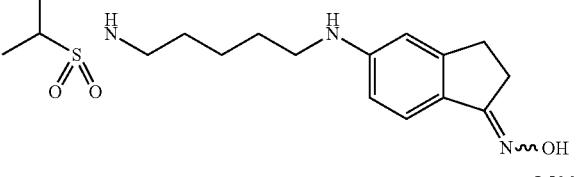
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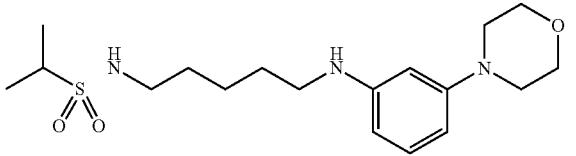
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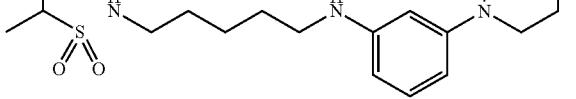
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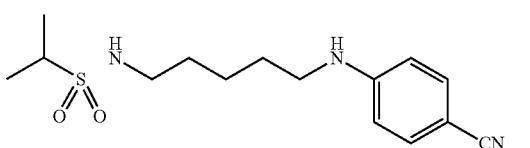
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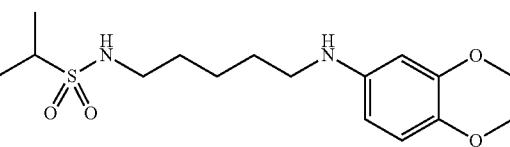
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**116**

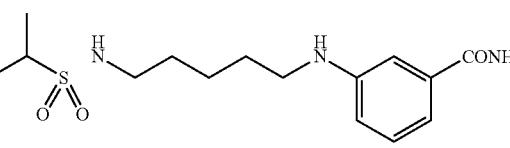
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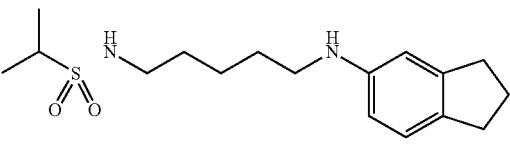
I-508



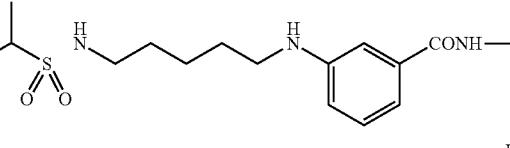
I-509



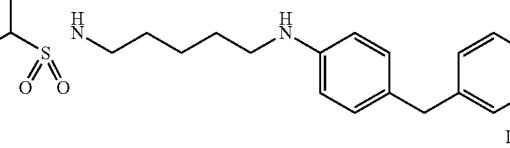
I-510



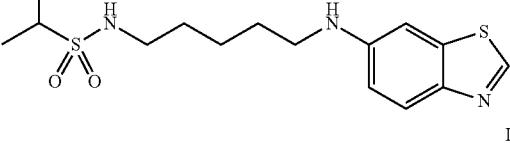
I-511



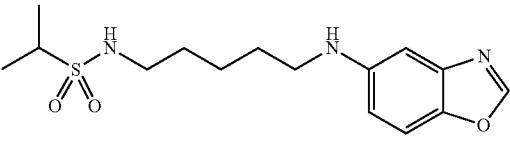
I-512



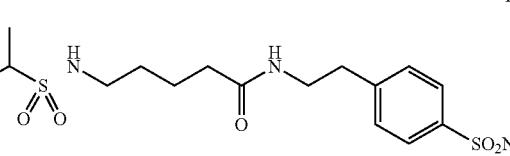
I-513



I-514



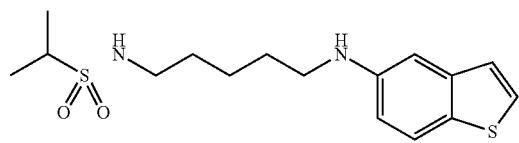
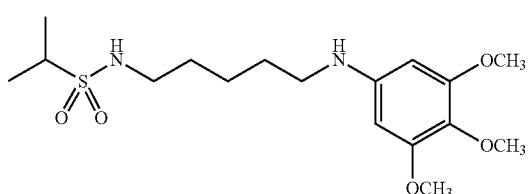
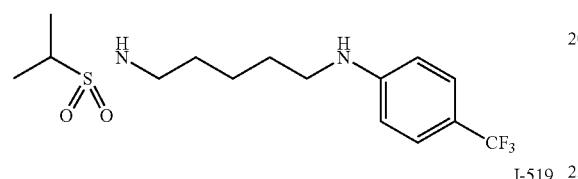
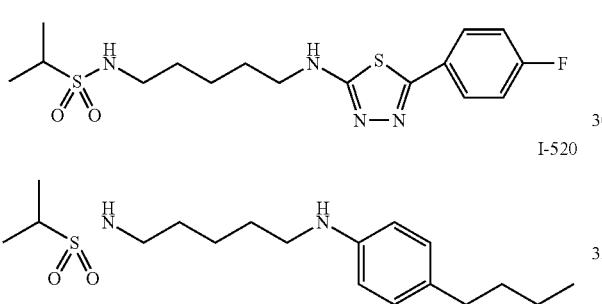
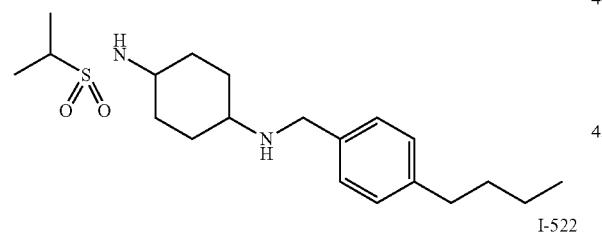
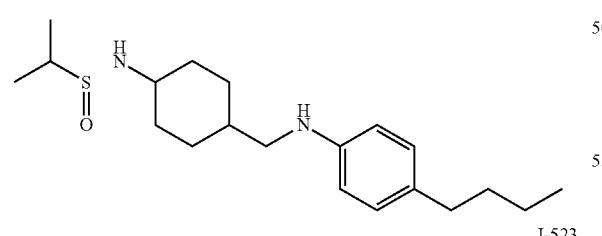
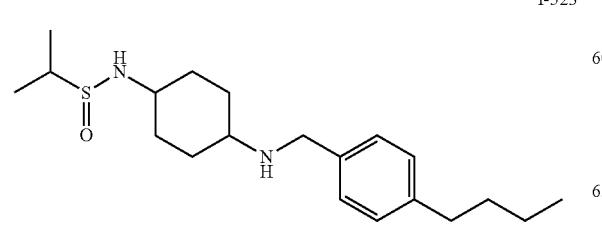
I-515



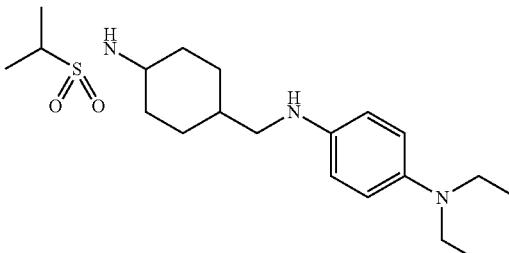
I-515

117
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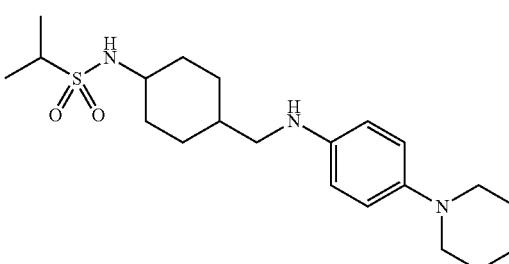
I-516

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I-517
10I-518
20I-519
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30I-521
35I-522
45I-523
55I-524
60**118**
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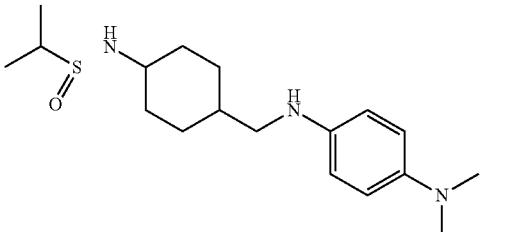
I-524



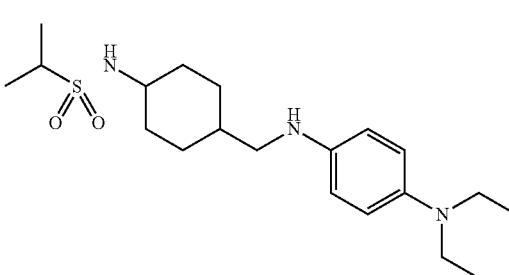
I-525



I-526



I-527

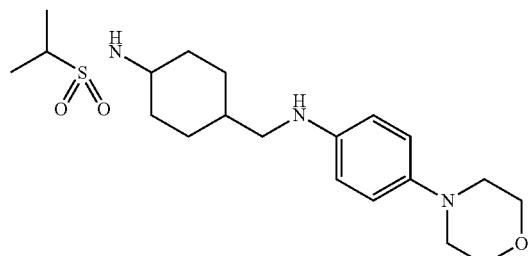


I-528

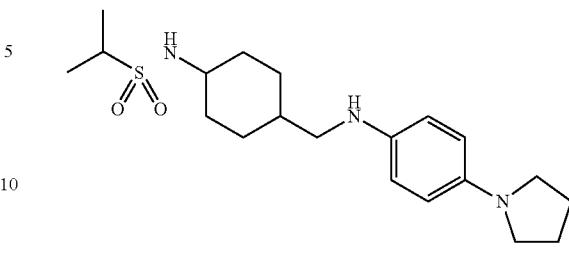
[Formula 94]

119
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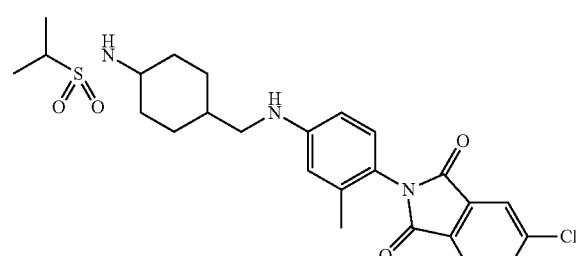
I-529



I-530

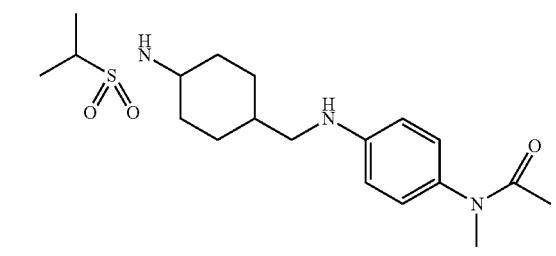


I-535



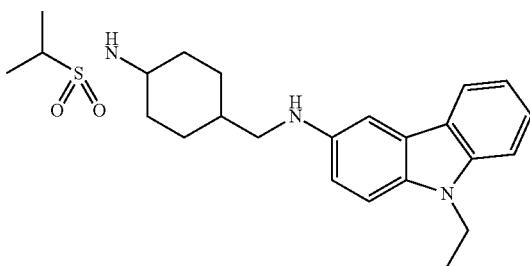
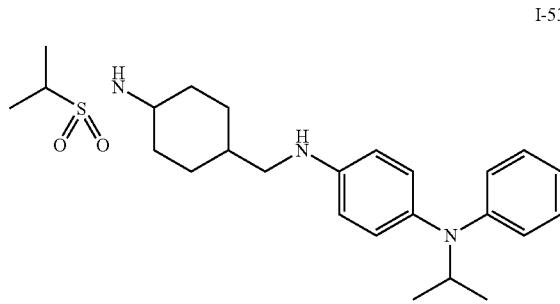
I-531

I-536



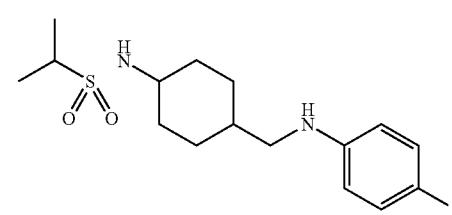
I-532

I-537



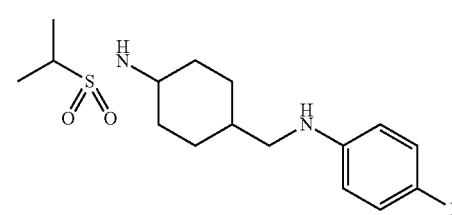
I-533

I-538



I-534

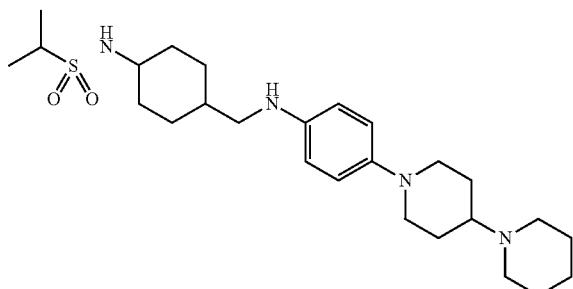
I-539



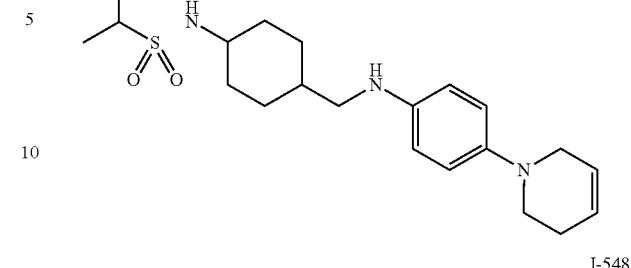
I-535

121

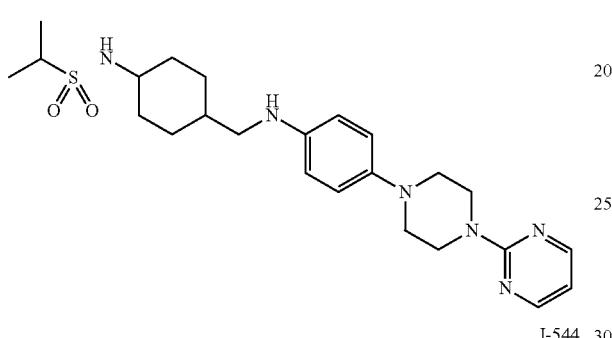
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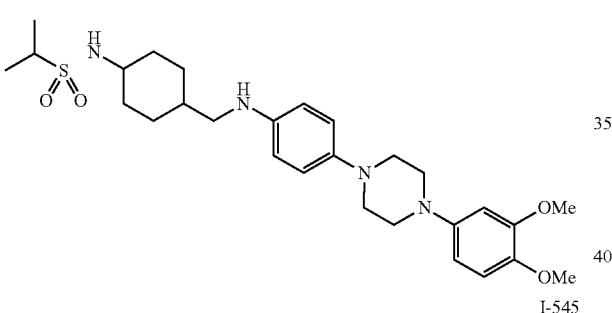
[Formula 95]



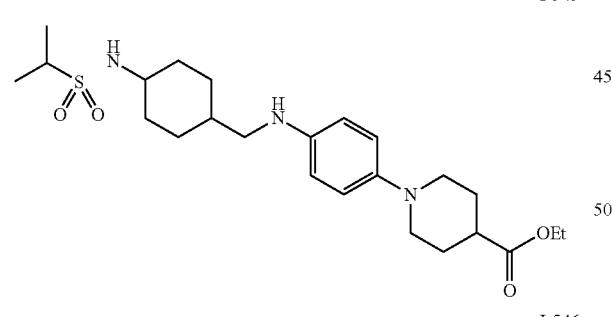
I-543



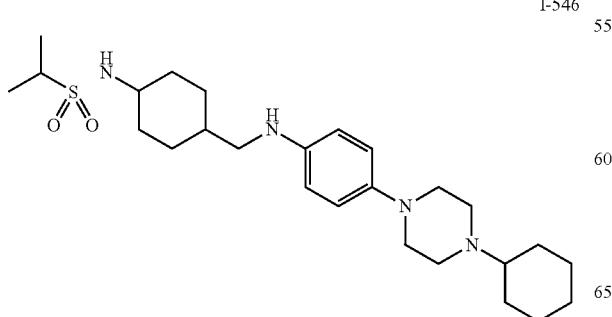
I-545



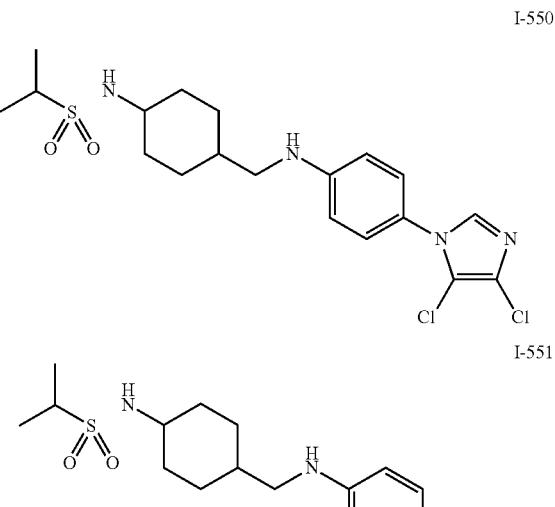
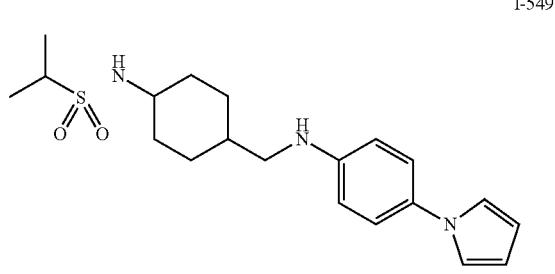
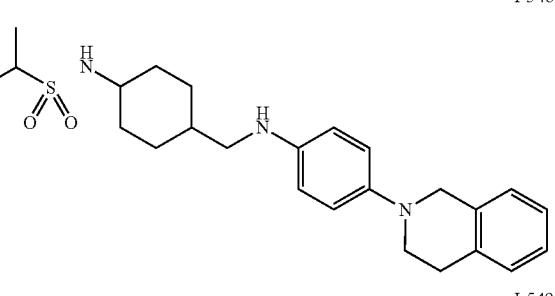
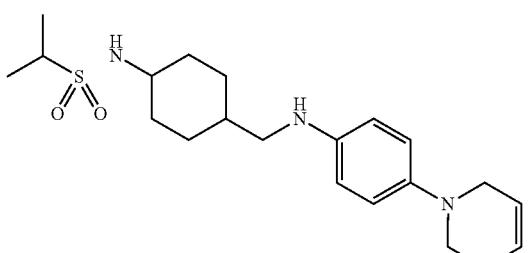
I-546



I-547

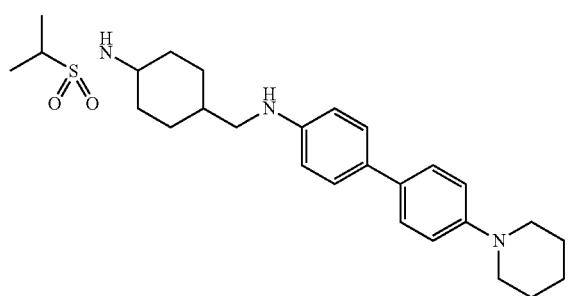
**122**

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123
-continued

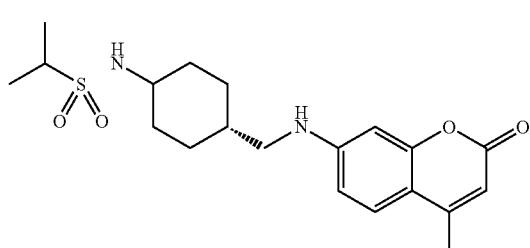
I-553



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I-554

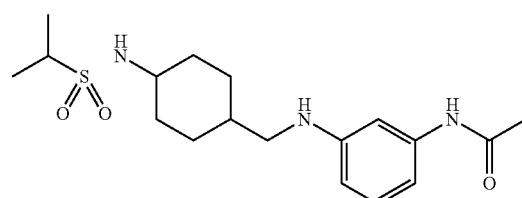


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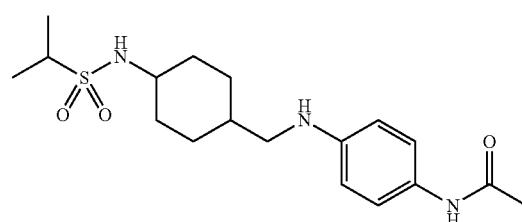
I-555



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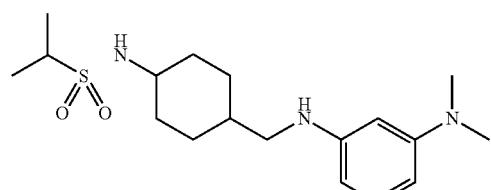
I-556



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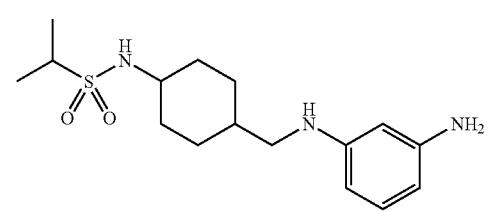
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I-557



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I-558



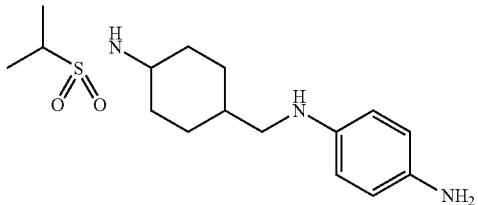
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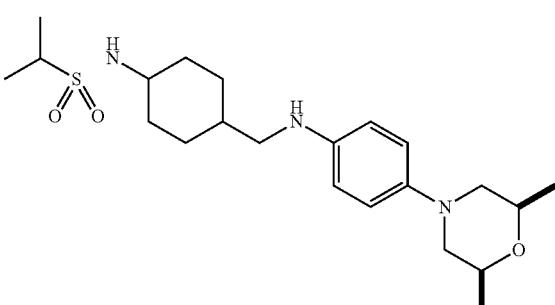
65

124
-continued

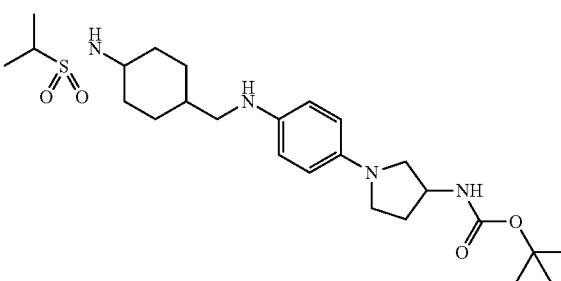
I-559



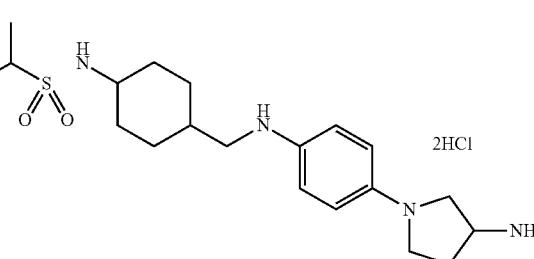
I-560



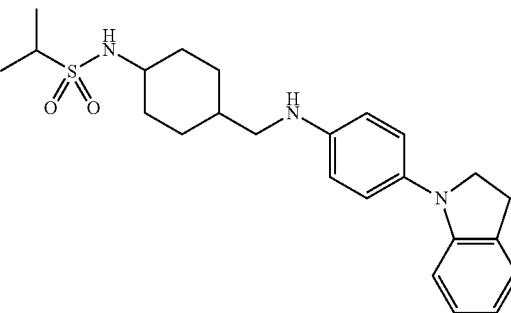
I-561



I-562

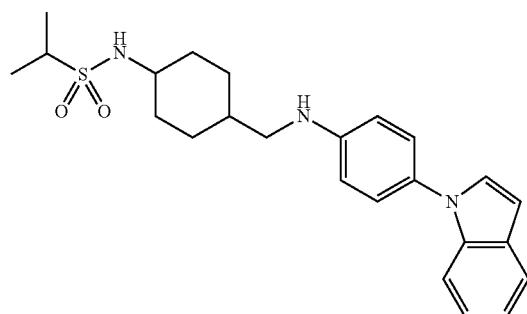


I-563



125

-continued

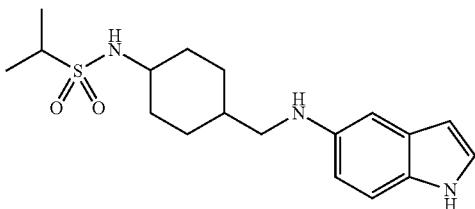


[Formula 96]

I-564

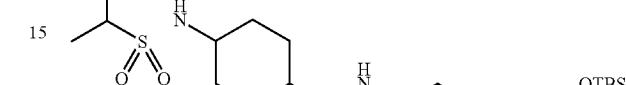
126

-continued

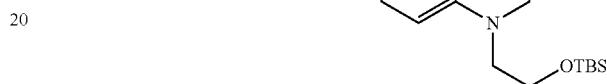


I-569

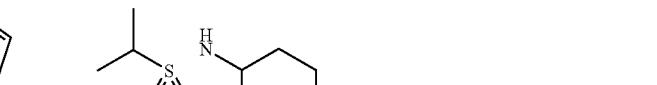
10 I-570



I-565



I-571



I-566

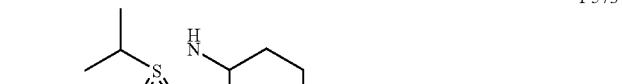


I-572

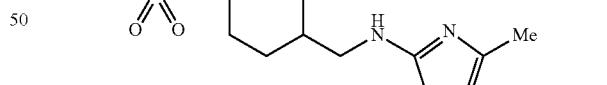


I-567

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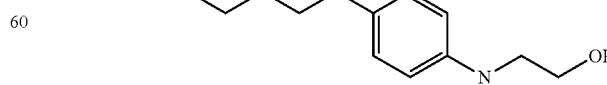
I-573



I-574



I-568

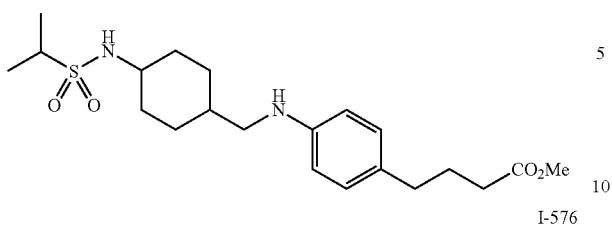


I-569

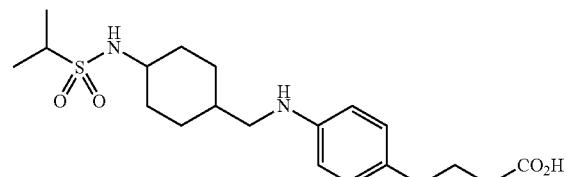
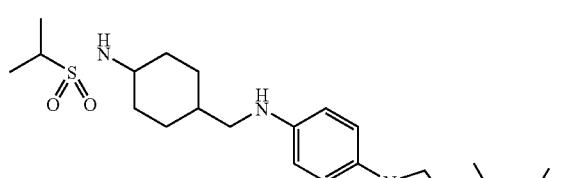


I-570

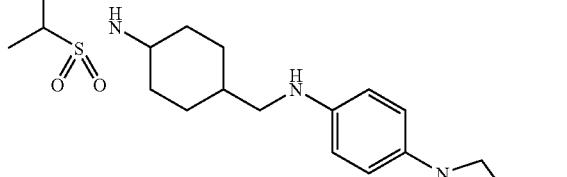
127
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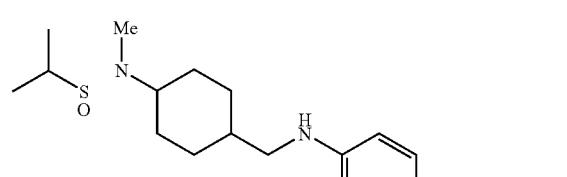
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I-57615
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I-578

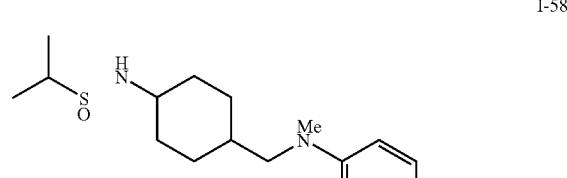
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I-579

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I-580

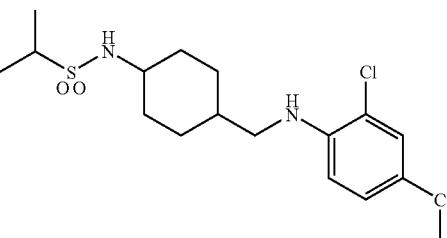
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I-581

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128
-continued

I-582



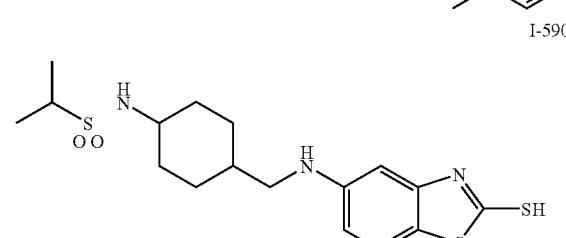
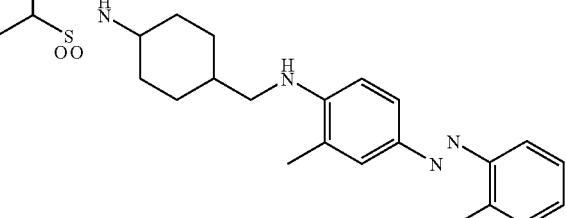
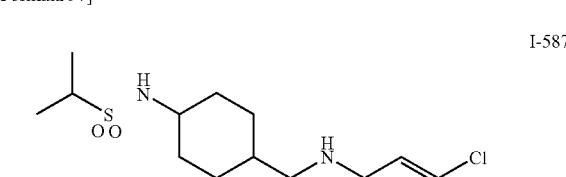
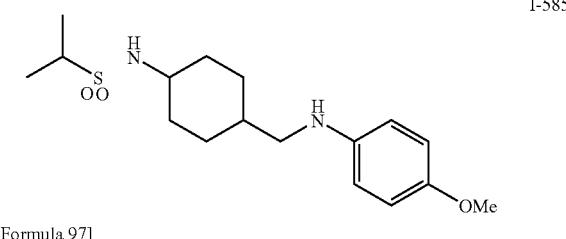
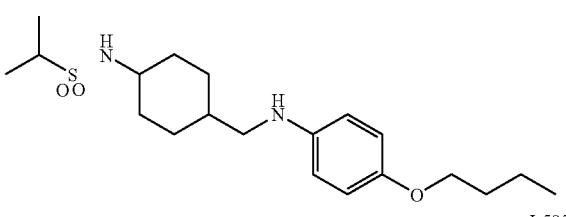
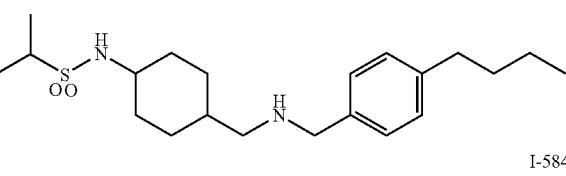
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I-576

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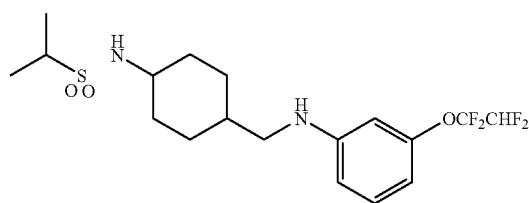
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I-577

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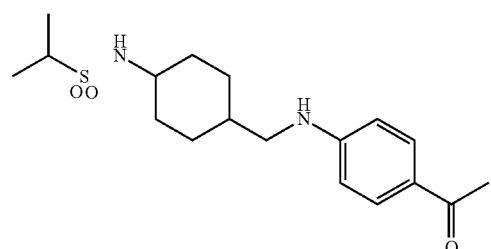
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I-57835
[Formula 97]40
I-57945
I-58050
I-58155
I-58260
I-58365
I-584

129
-continued

I-591

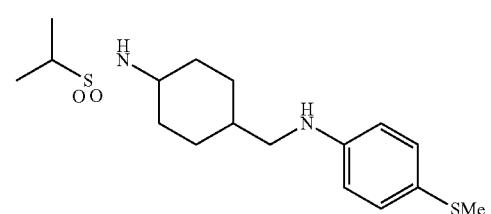


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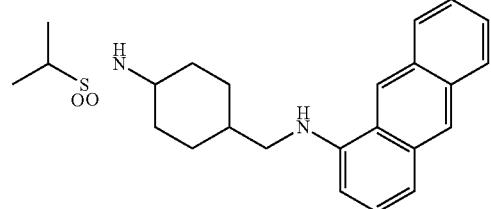
I-592

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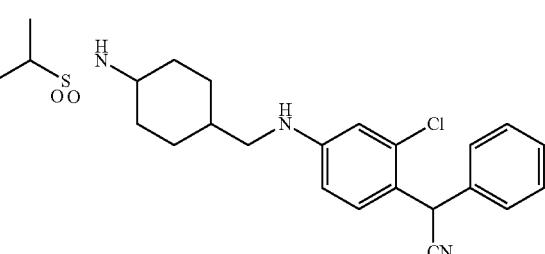
I-593

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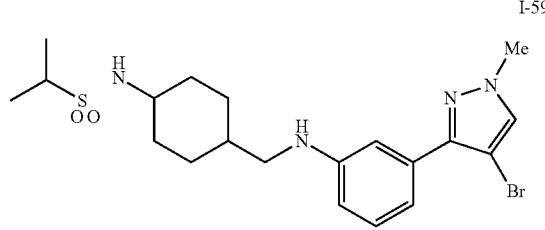
I-594

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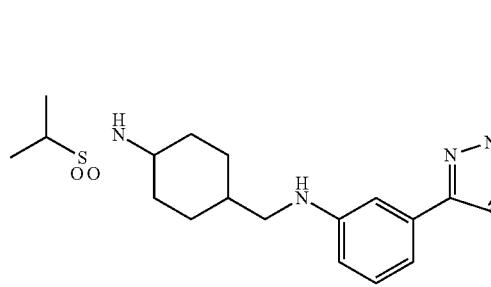
I-595

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I-596

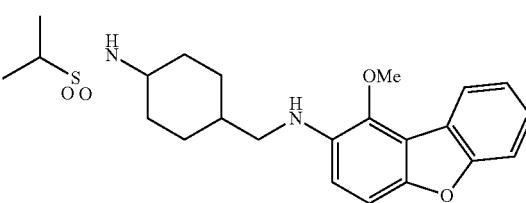
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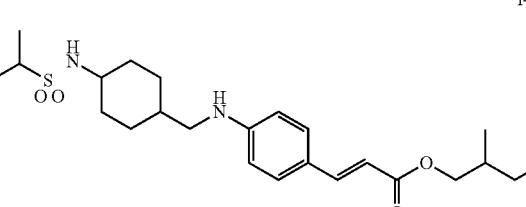
130
-continued

I-598

I-597

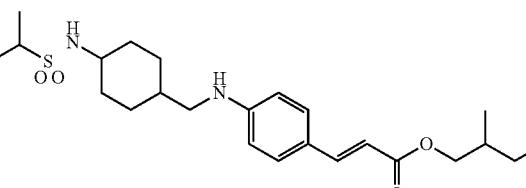


5

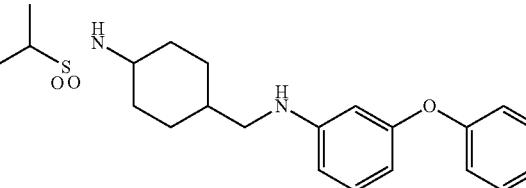


I-598

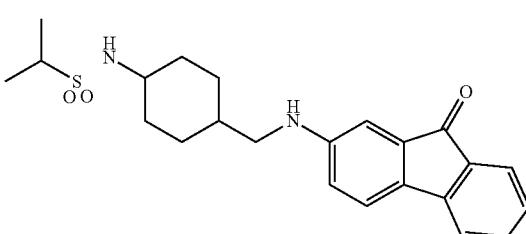
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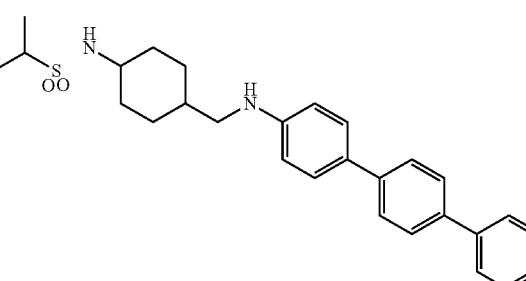
I-599



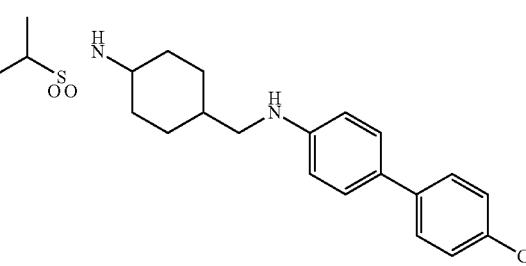
I-600



I-601



I-602

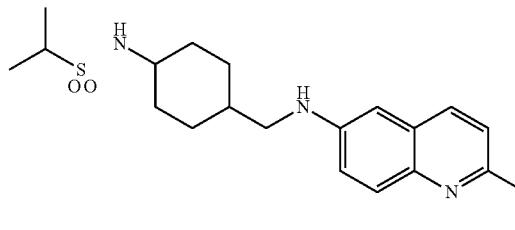
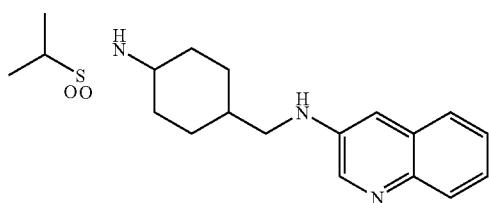
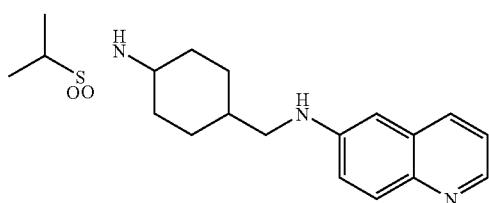
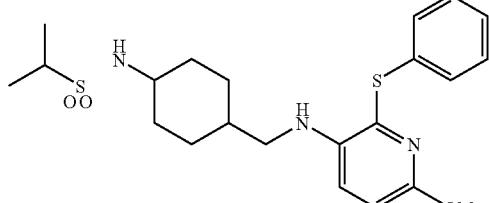
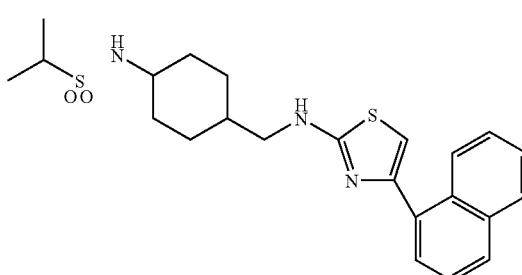
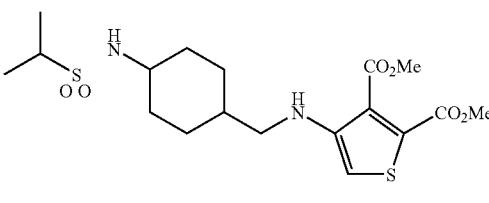
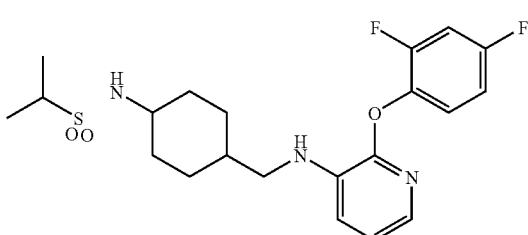


131

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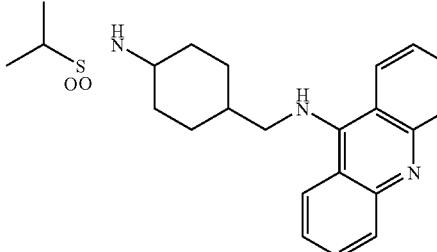
I-603

[Formula 98]

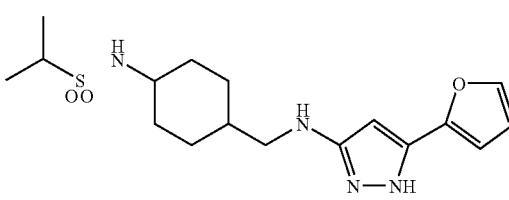
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I-60415
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I-60525
I-60630
I-60740
I-60850
I-60960
I-610**132**

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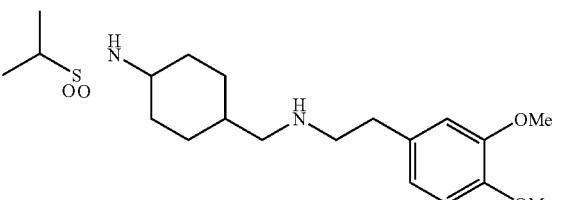
I-610



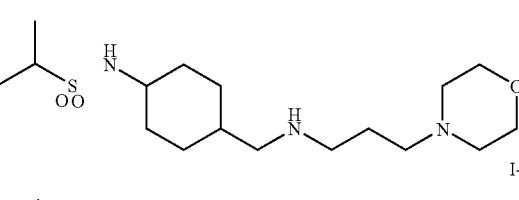
I-611



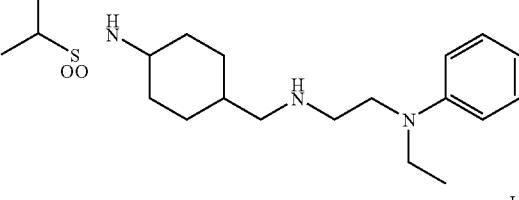
I-612



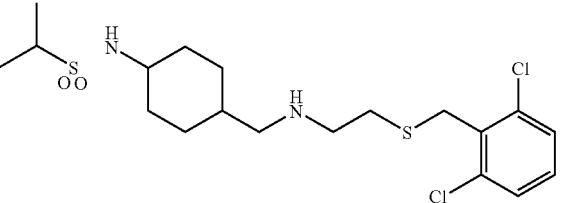
I-613



I-614



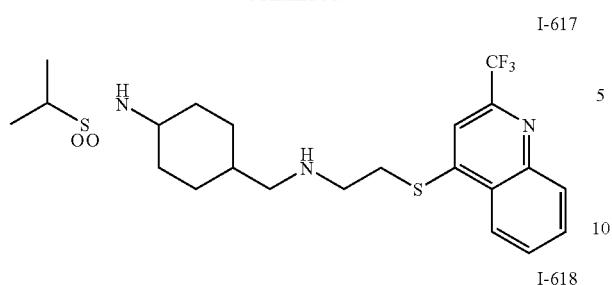
I-615



I-616

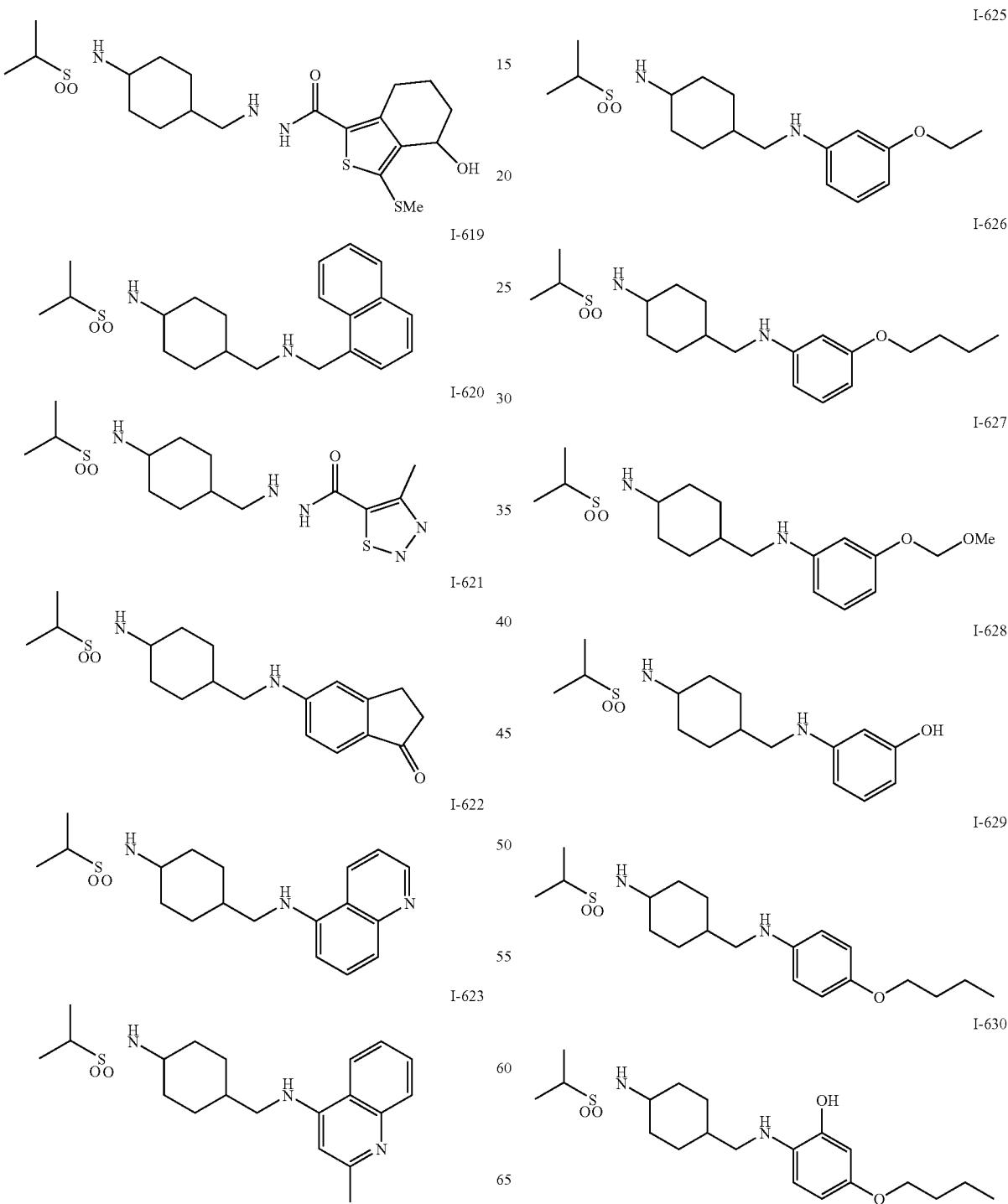
133

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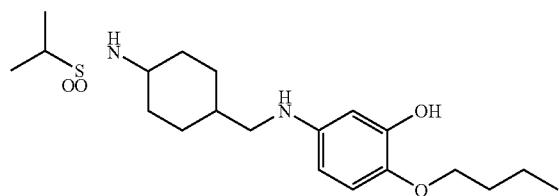
134

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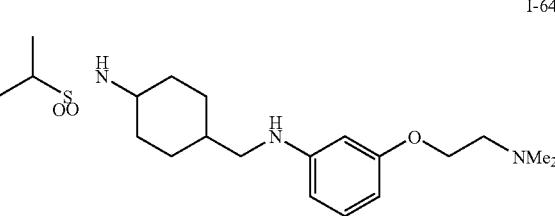
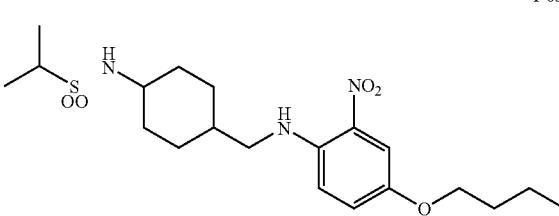
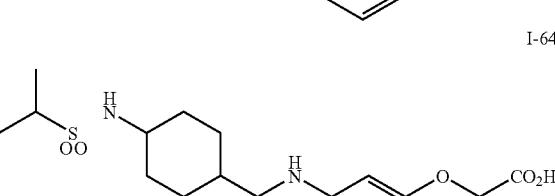
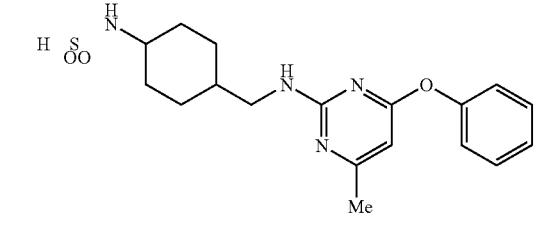
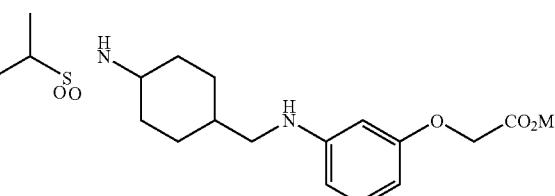
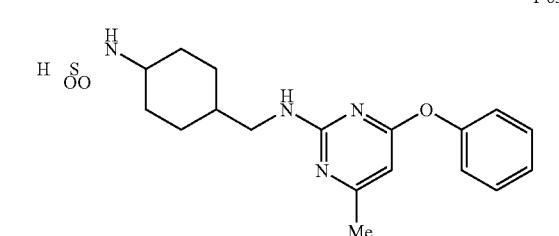
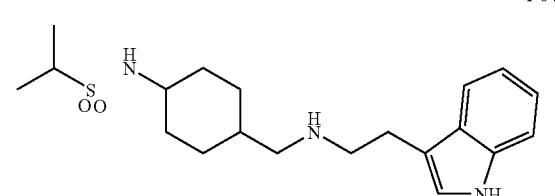
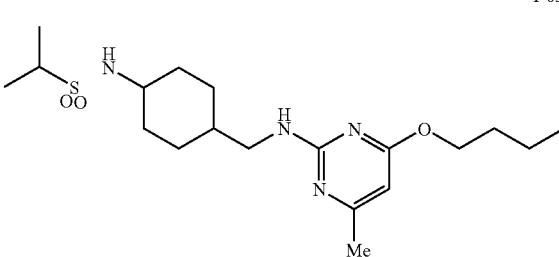
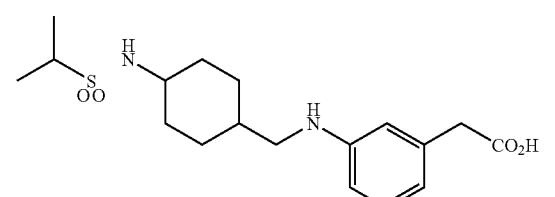
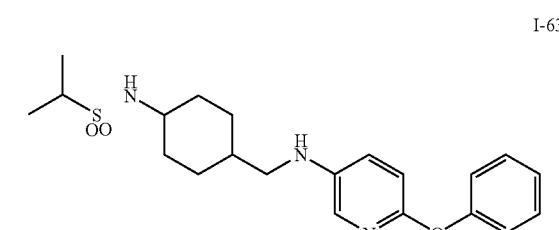
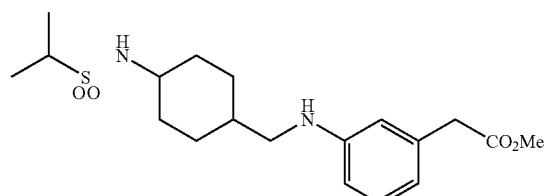
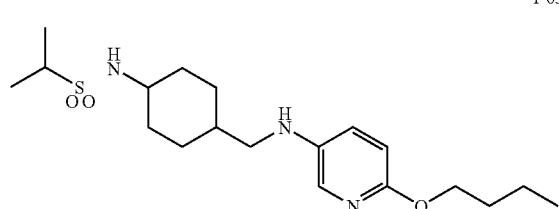
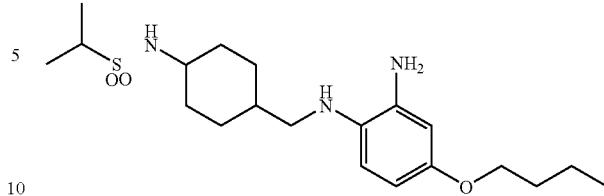


135

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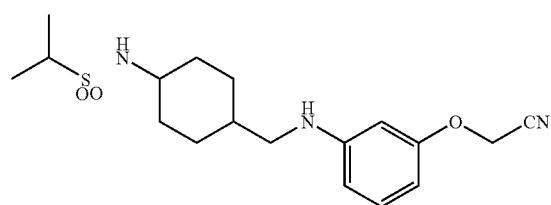
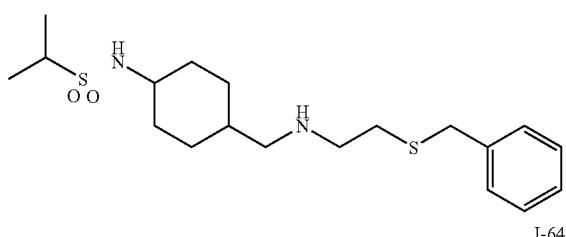
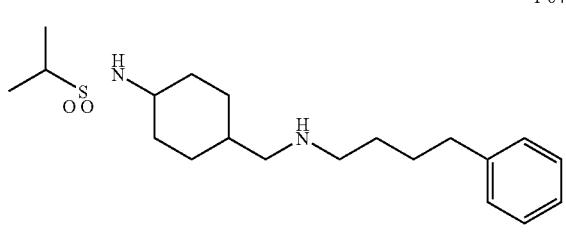
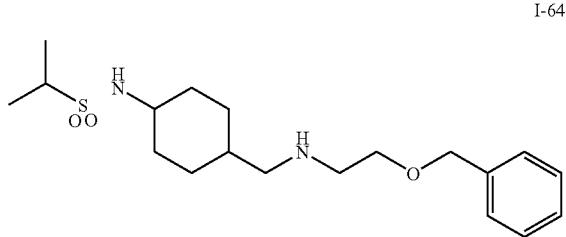
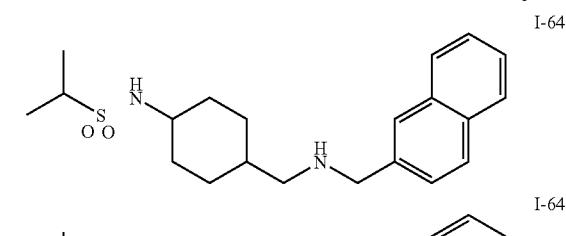
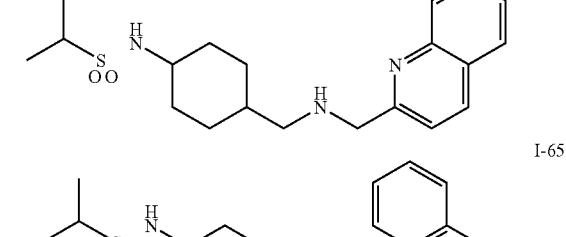
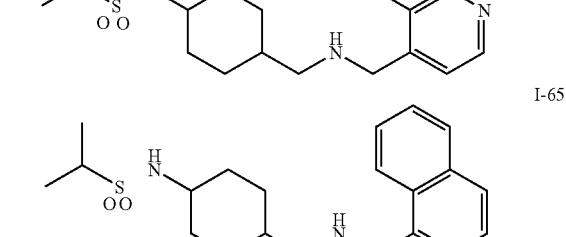
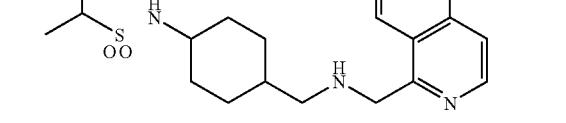


[Formula 99]



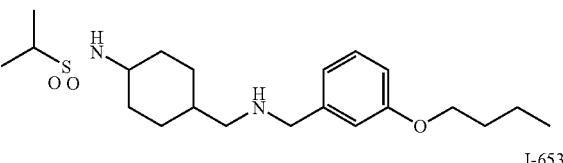
137
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I-644

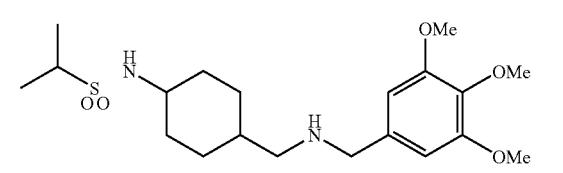
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I-64515
I-64620
I-64725
I-64830
I-64935
I-65040
I-651

138
-continued

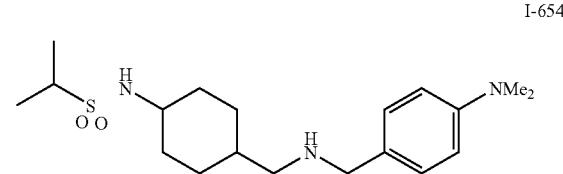
I-652



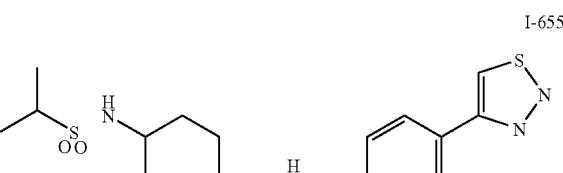
I-653



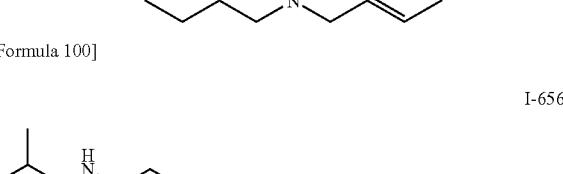
I-654



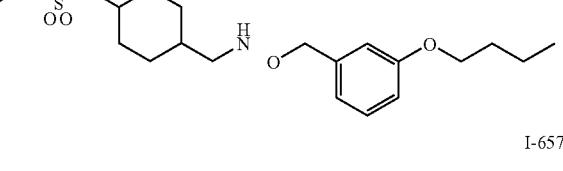
I-655



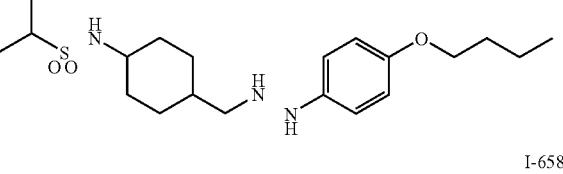
I-656



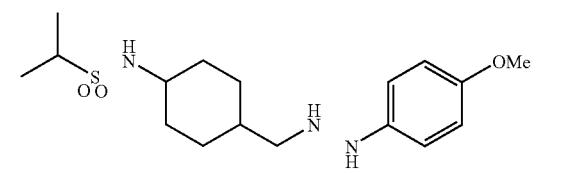
I-657



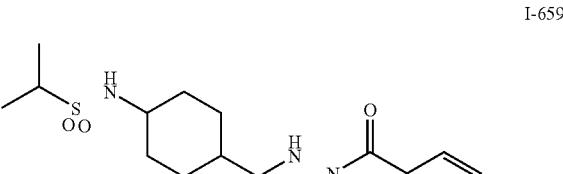
I-658



I-659



I-660



I-661

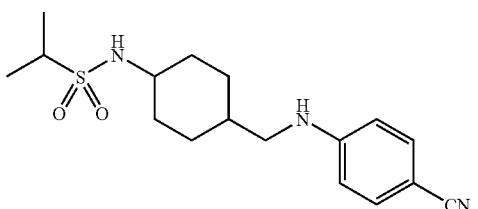
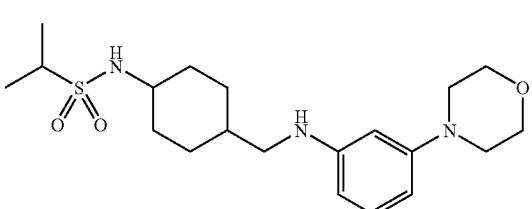
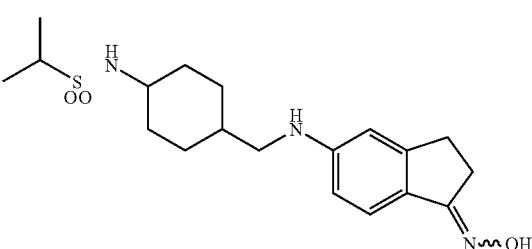
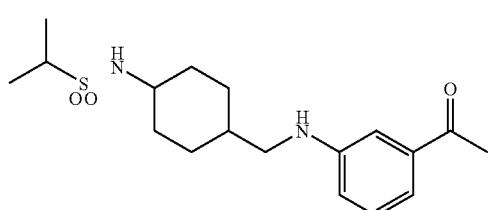
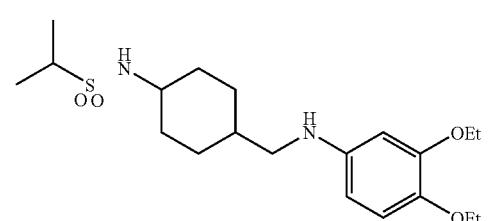
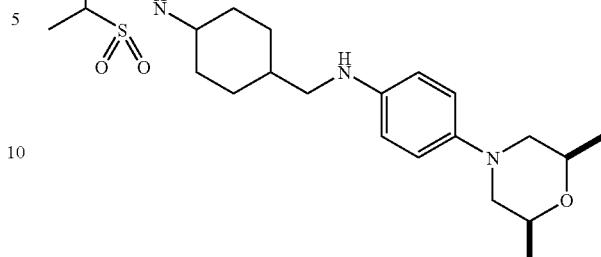
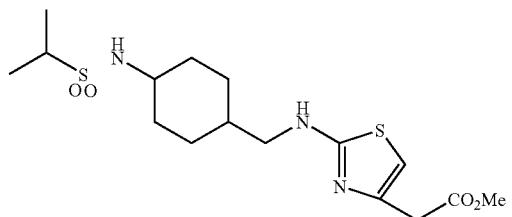


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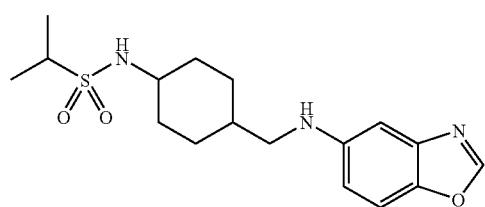
139

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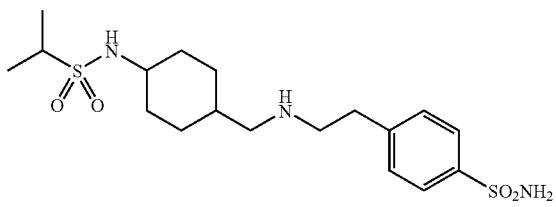
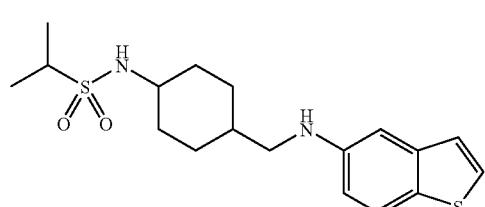
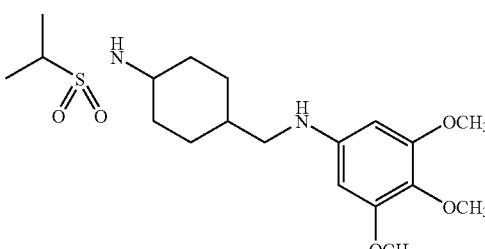
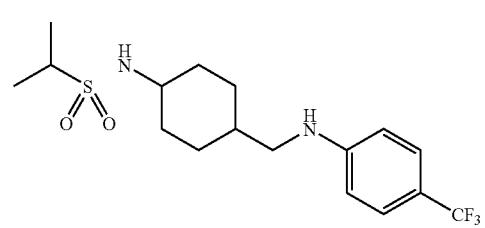
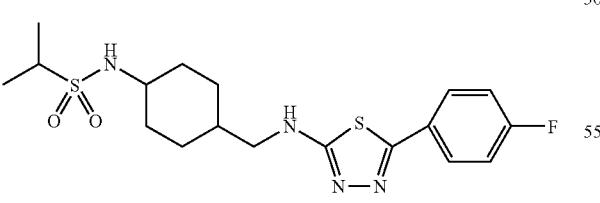
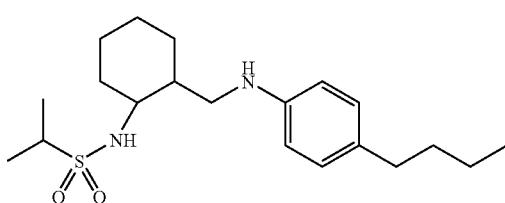
141

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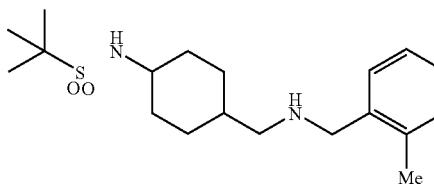
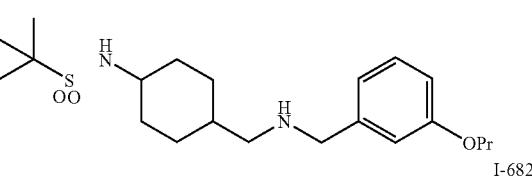


I-673

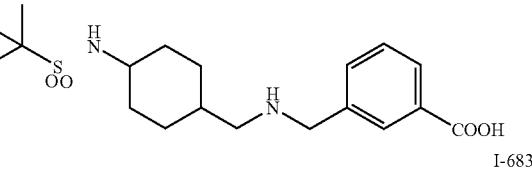
[Formula 101]

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I-67415
2025
I-675
I-67635
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I-67745
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I-678
I-67960
65**142**

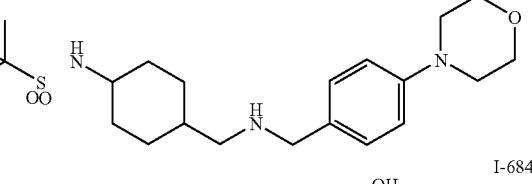
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I-680
I-681

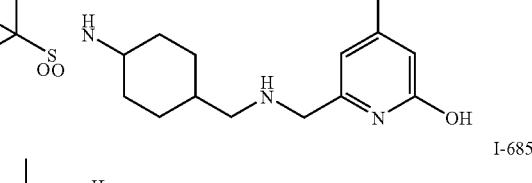
I-681



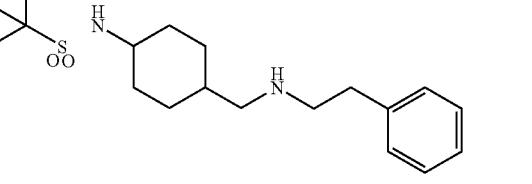
I-682



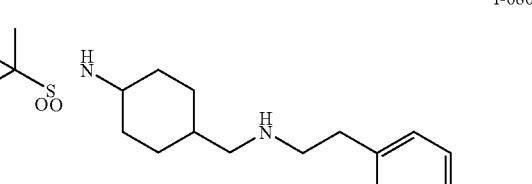
I-683



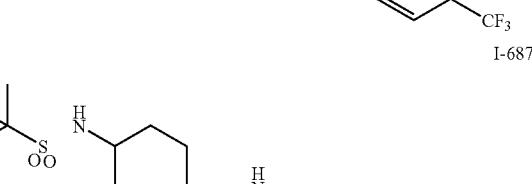
I-684



I-685



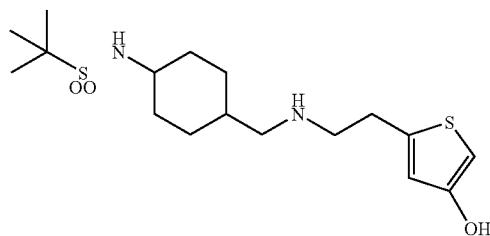
I-686



I-687

143

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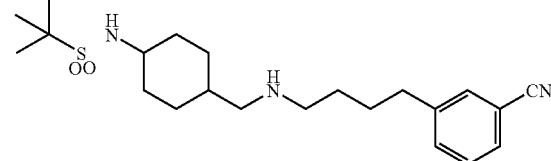


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144

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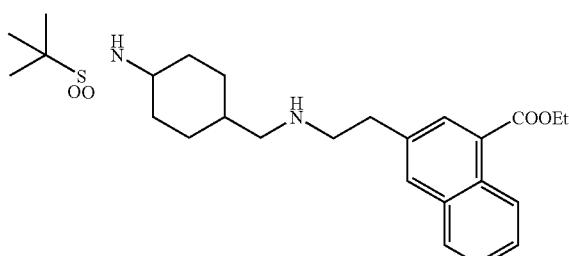
I-696



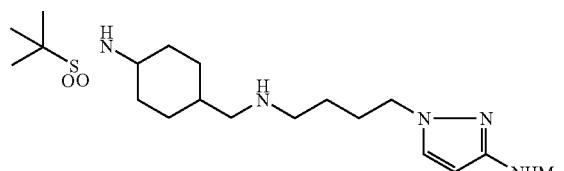
I-689

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I-697



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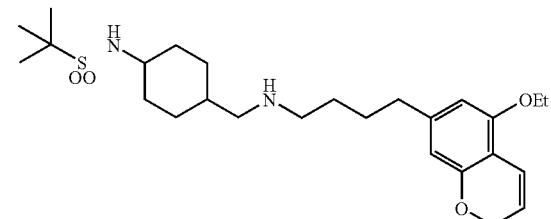
I-698

I-691

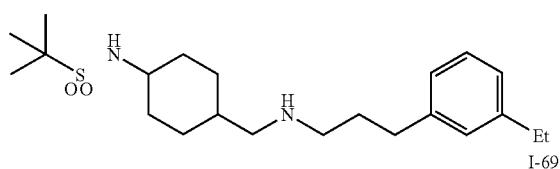
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I-691

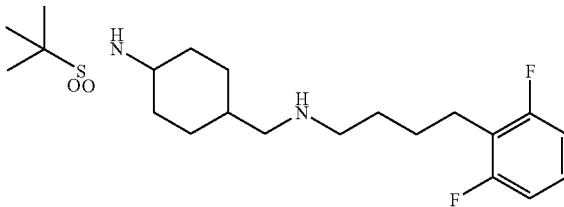
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I-699



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I-700

I-693

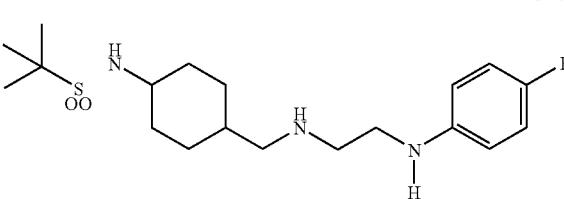
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I-694

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I-694

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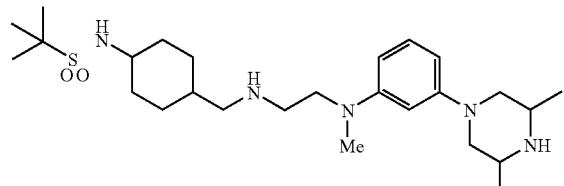
I-701

I-695

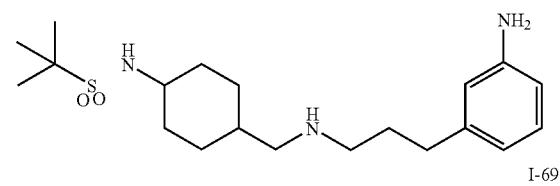
55

I-695

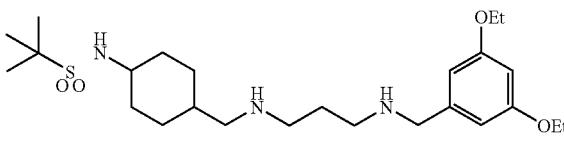
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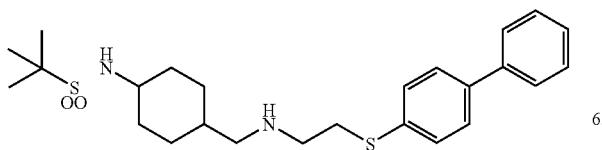
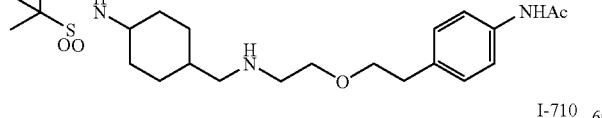
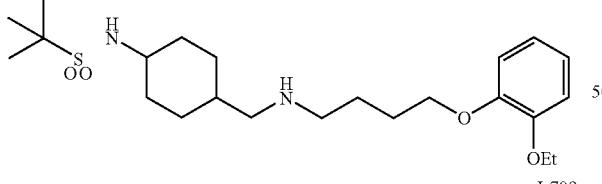
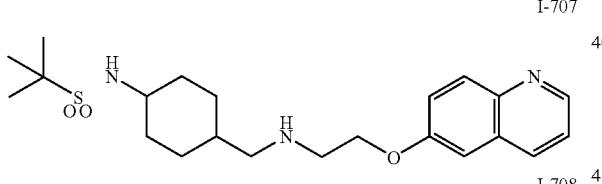
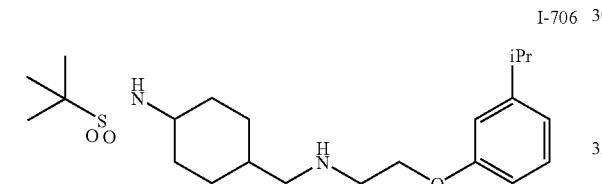
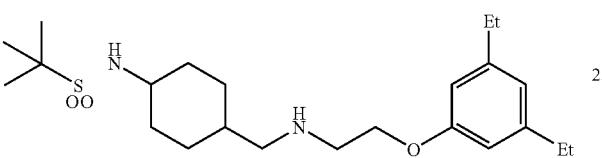
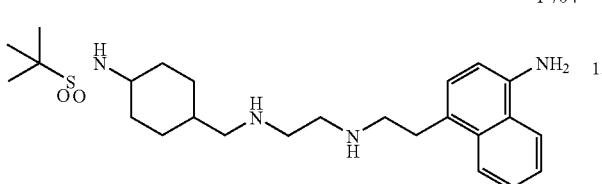
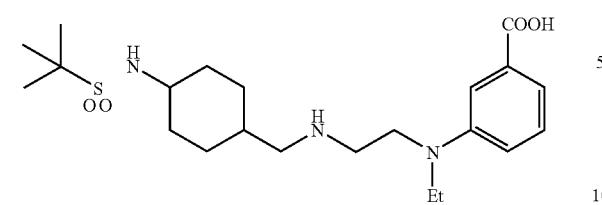
I-702



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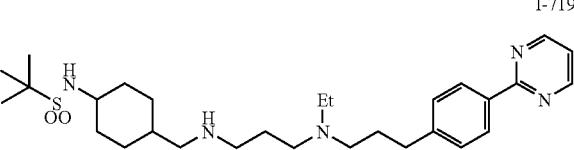
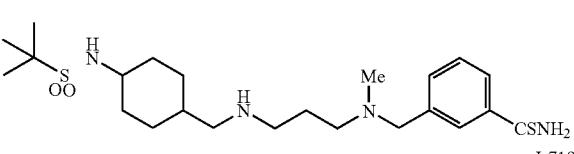
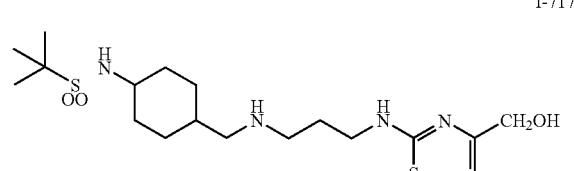
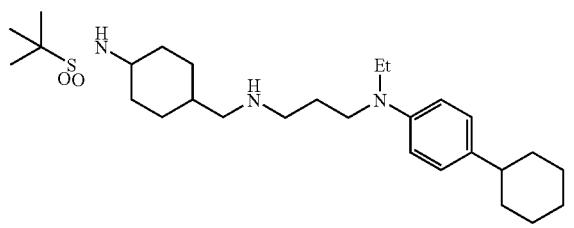
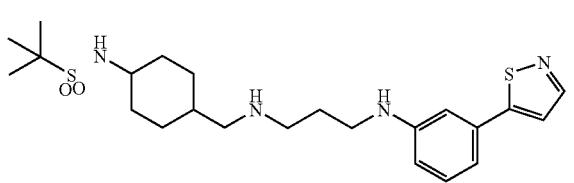
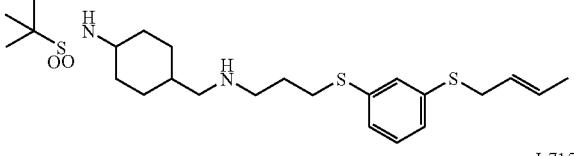
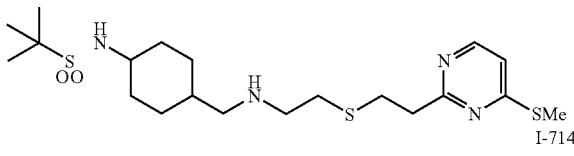
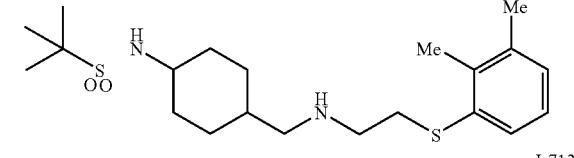
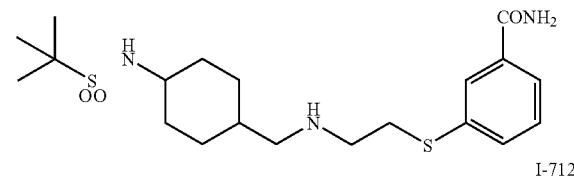


145
-continued



146
-continued

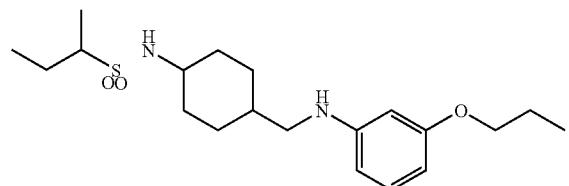
I-711



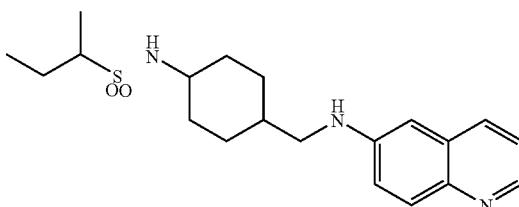
147

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[Formula 103]

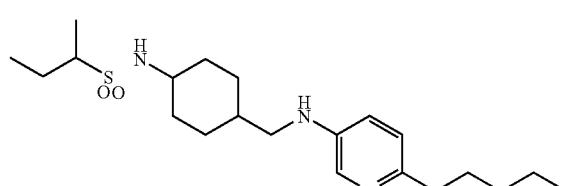


I-720

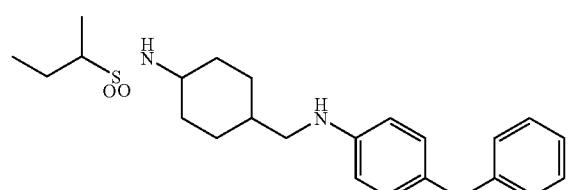
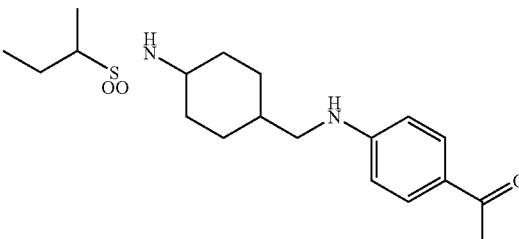
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10**148**

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I-726

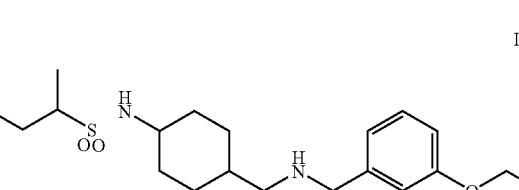


I-721

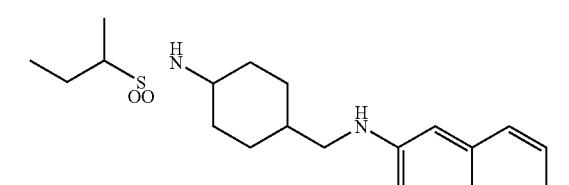
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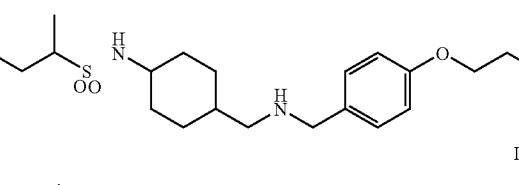


I-729

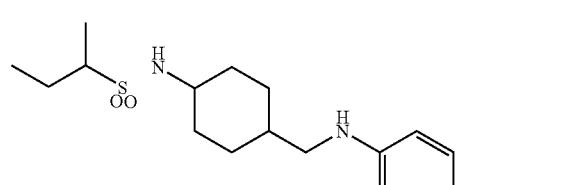


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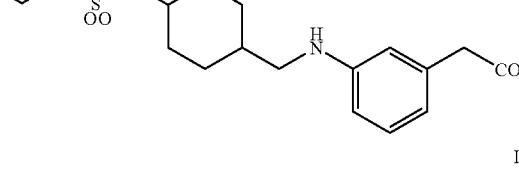


I-730

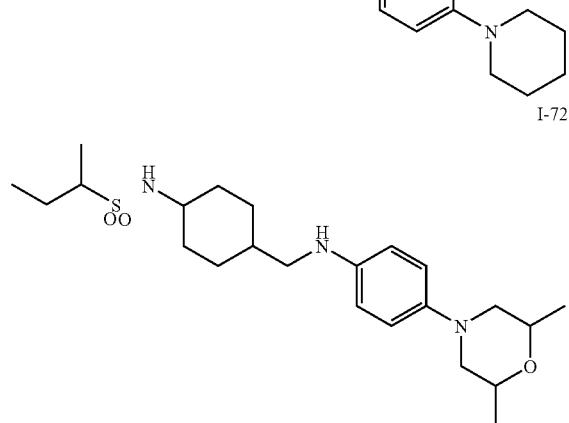


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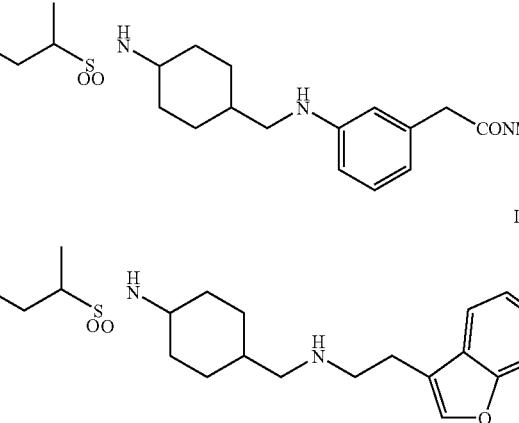


I-732



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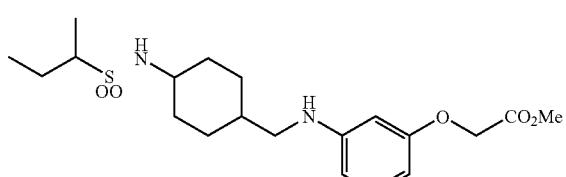
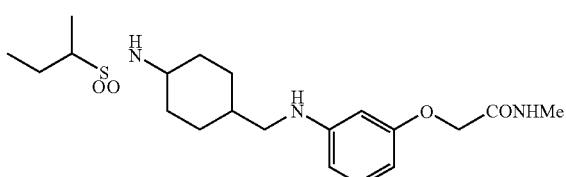
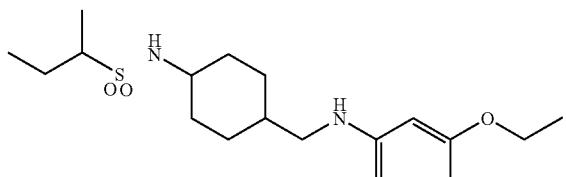
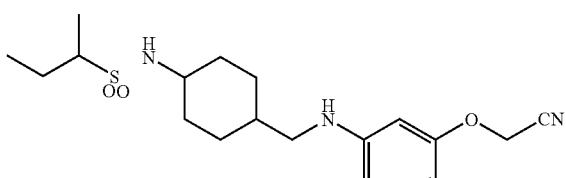
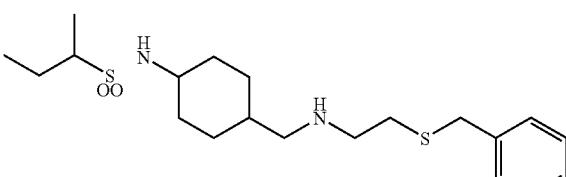
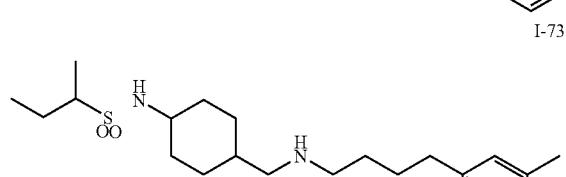
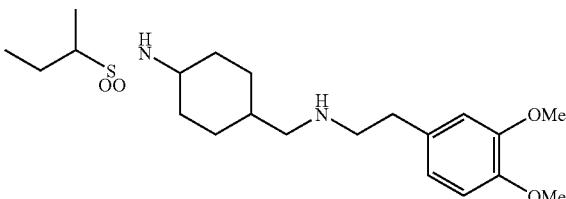


149

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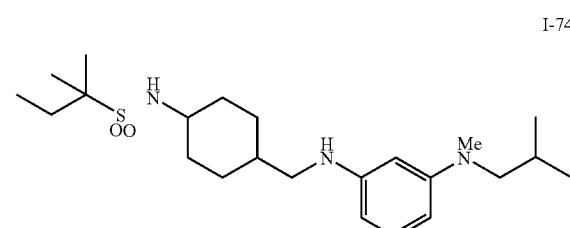
I-733

[Formula 104]

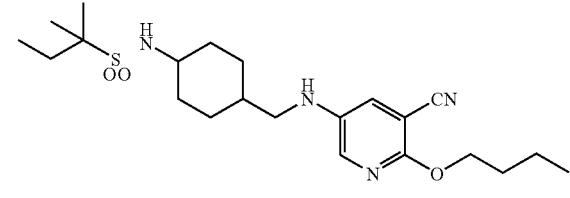
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I-73415
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I-73525
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I-73635
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I-73745
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I-73855
I-73960
65
I-740**150**

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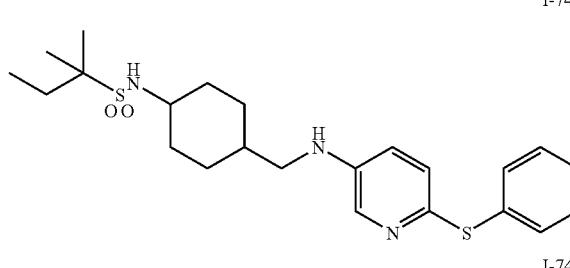
I-740



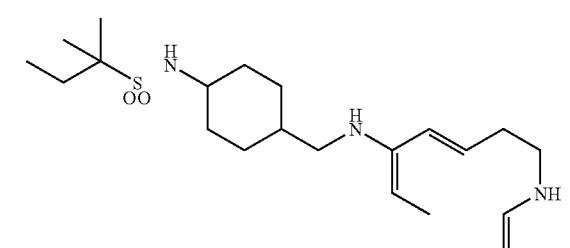
I-741



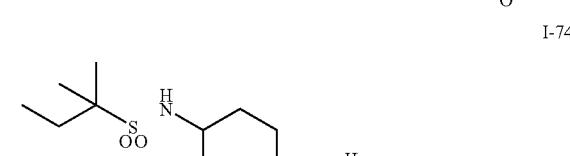
I-742



I-743

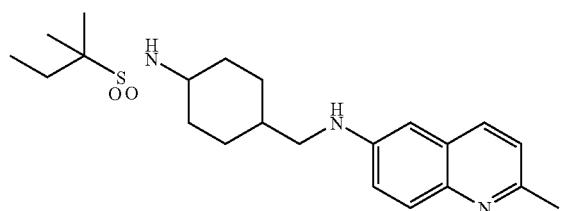


I-744

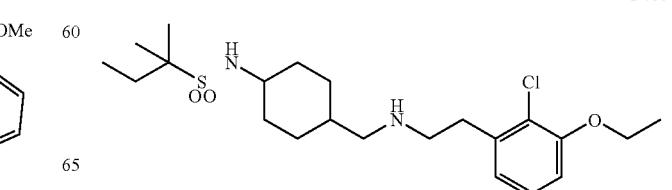
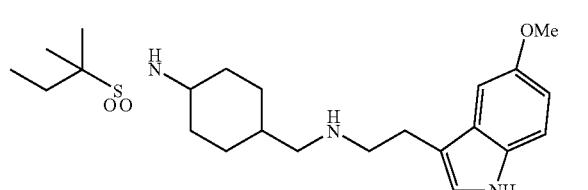
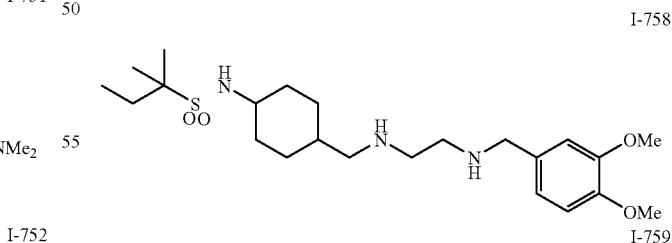
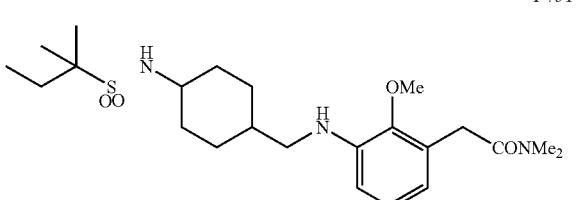
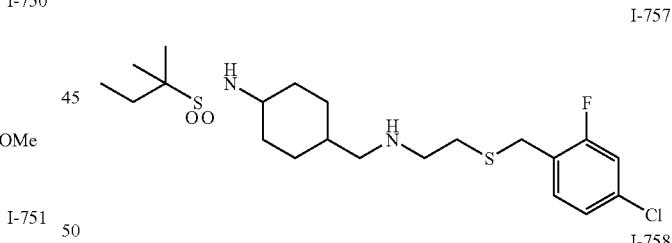
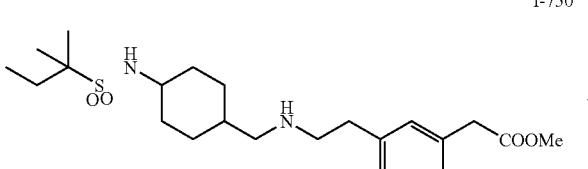
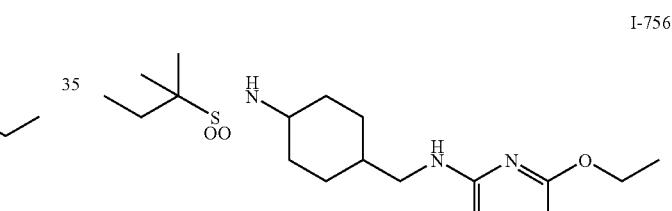
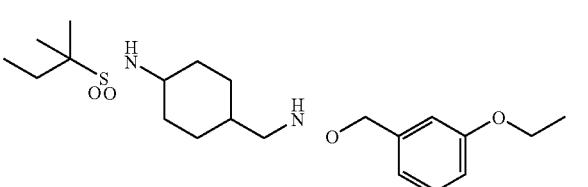
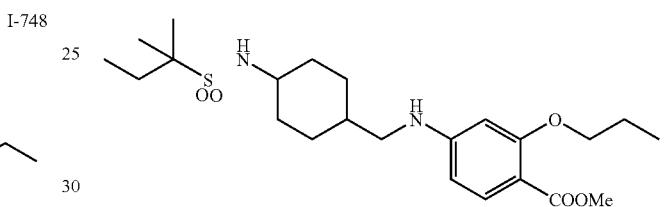
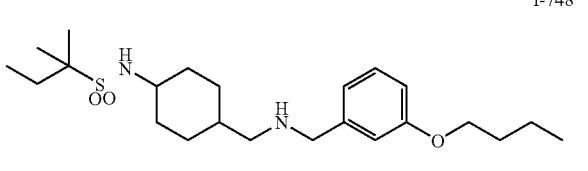
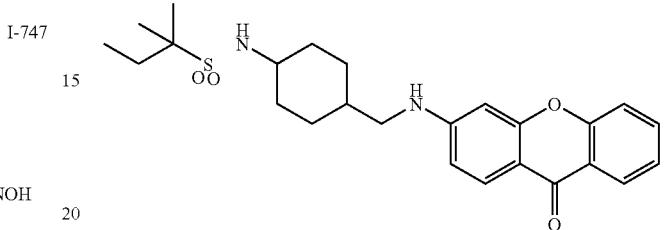
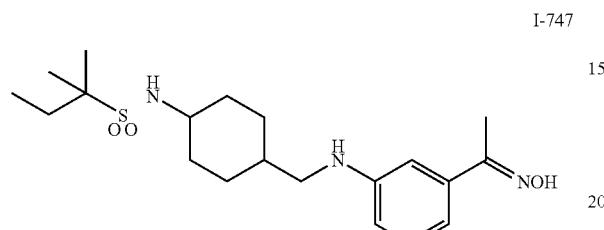
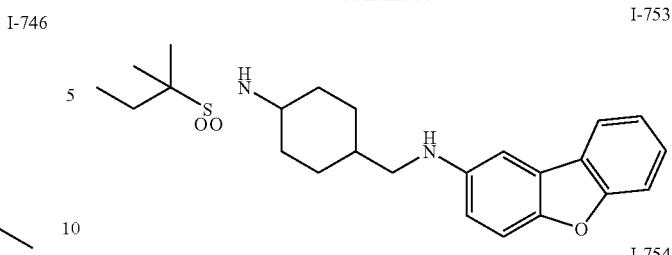


I-745

151



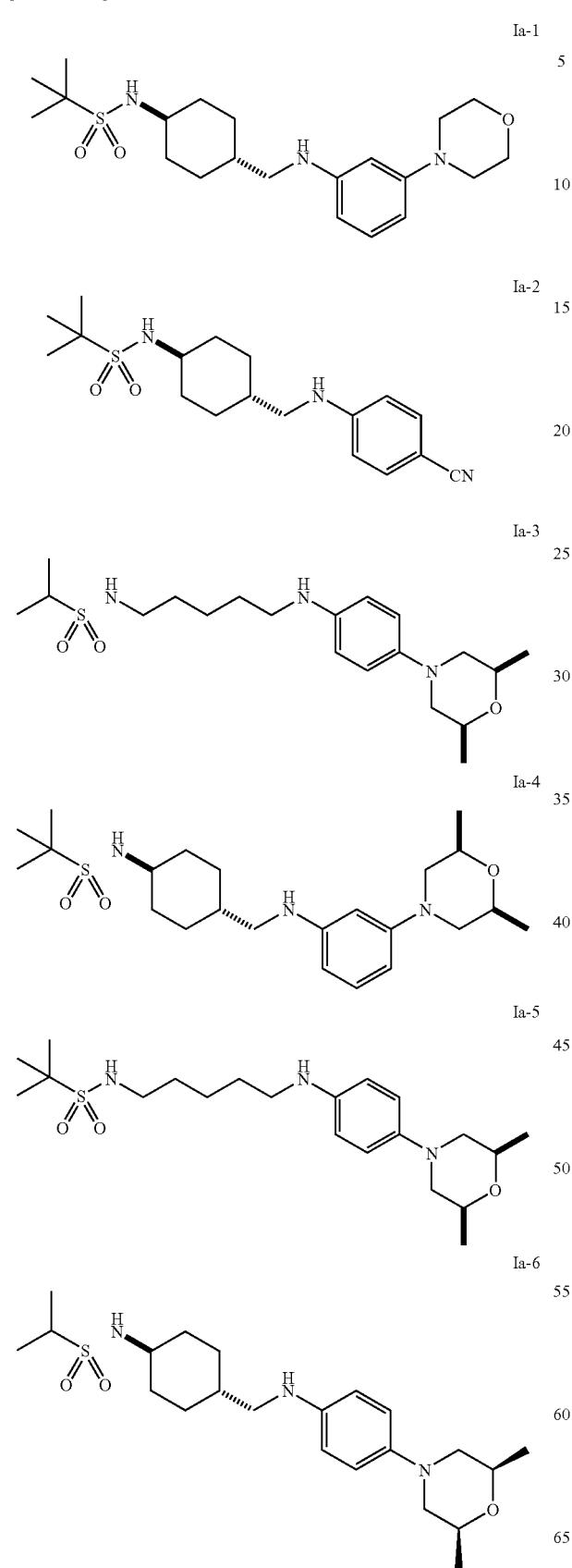
152



153

-continued

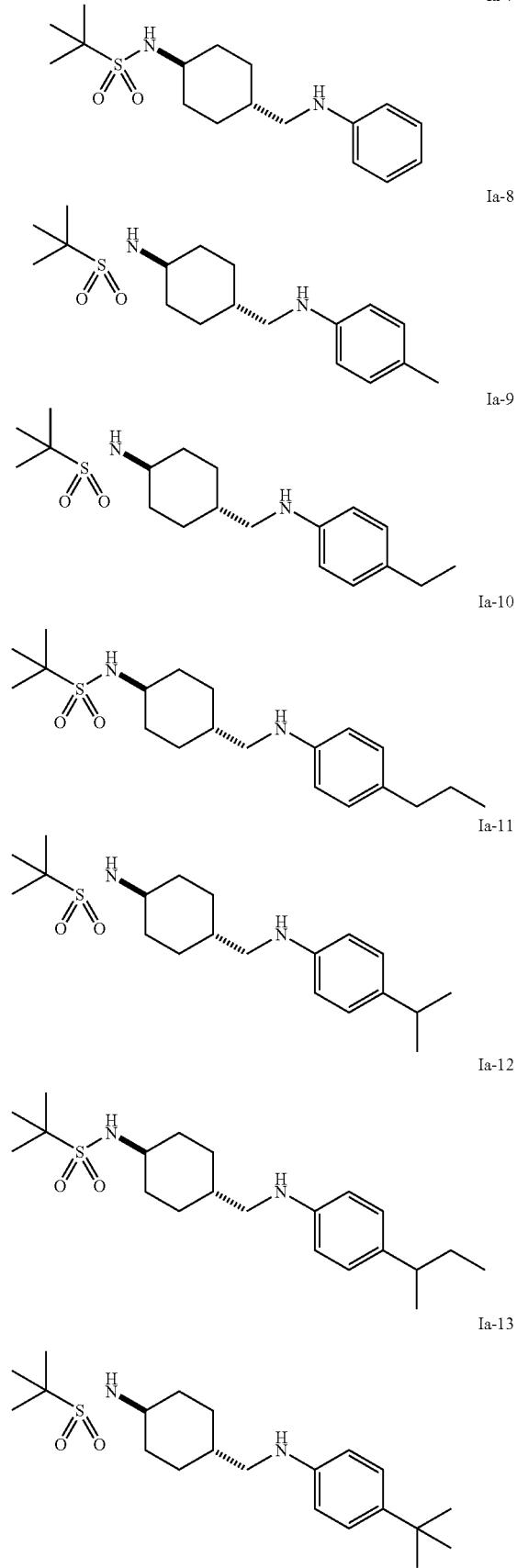
[Formula 105]



154

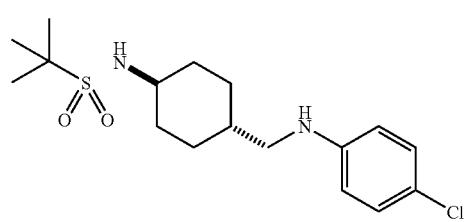
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Ia-7

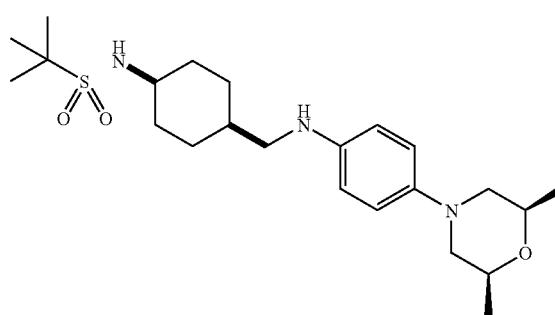
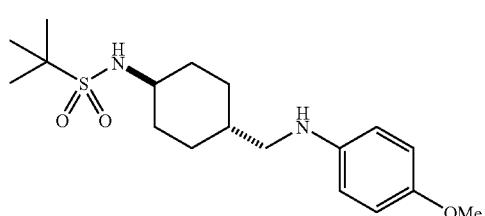
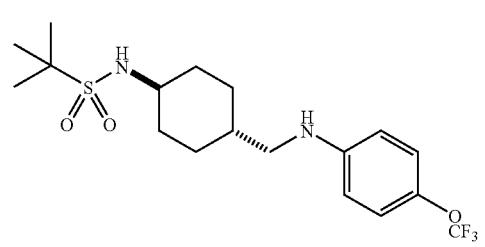
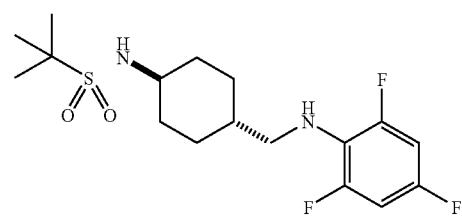
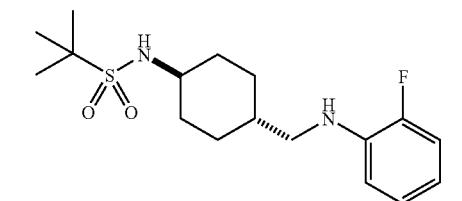
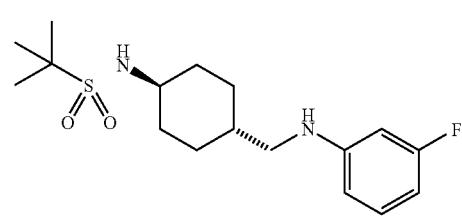
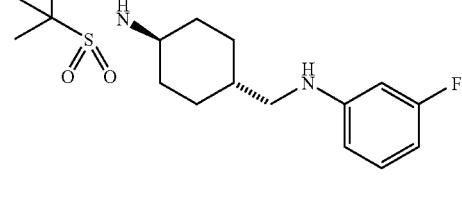
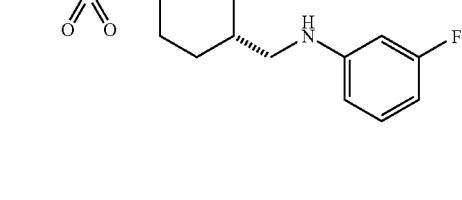


155

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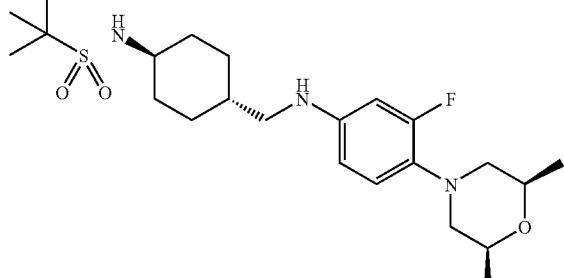
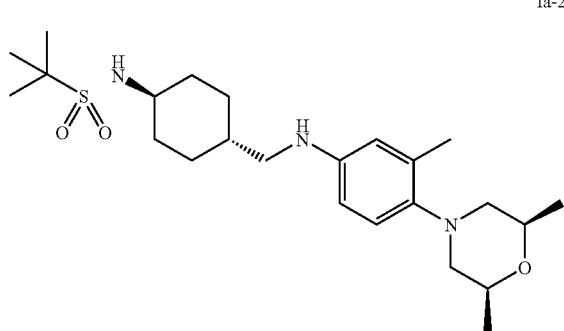
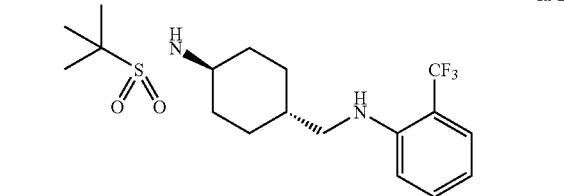
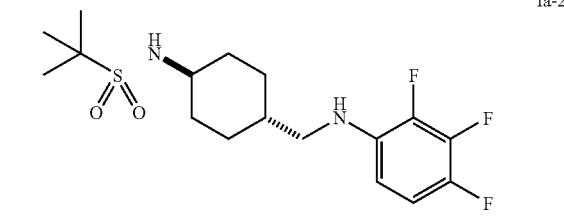
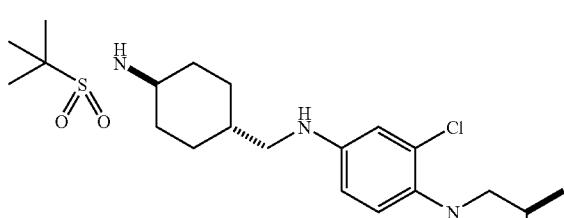
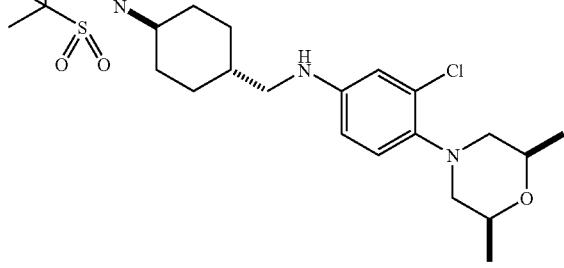


Ia-14

Ia-15
10Ia-16
15Ia-17
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[Formula 106]Ia-18
35Ia-19
45
50Ia-20
55Ia-20
60Ia-20
65**156**

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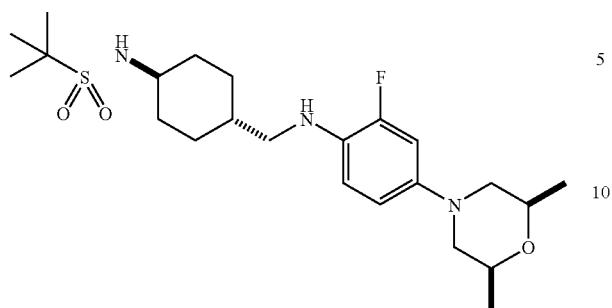
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Ia-22
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35Ia-24
45Ia-24
55Ia-25
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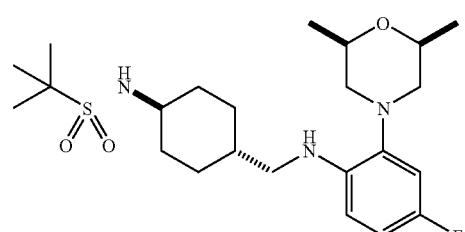
157

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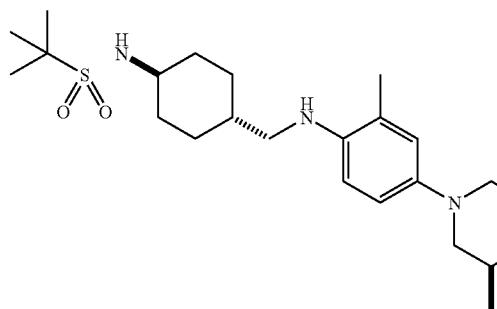
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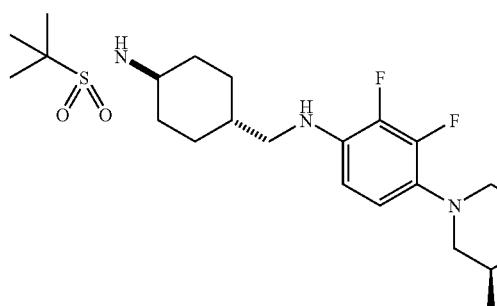
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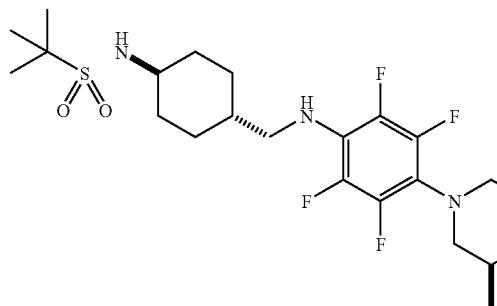
Ia-28



Ia-29

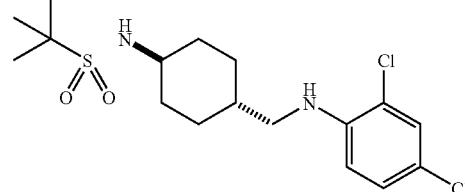


Ia-30

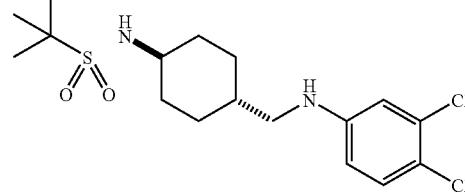
**158**

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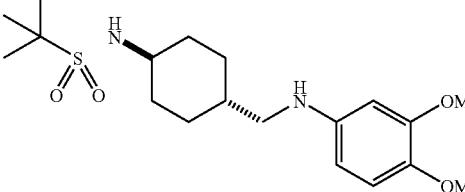
Ia-31



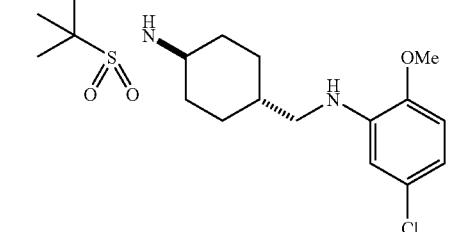
Ia-32



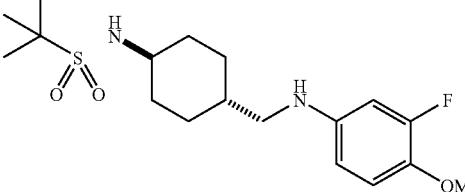
Ia-33



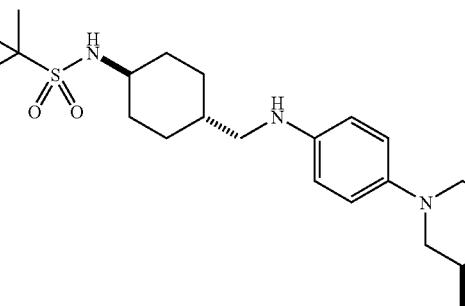
Ia-35



Ia-36

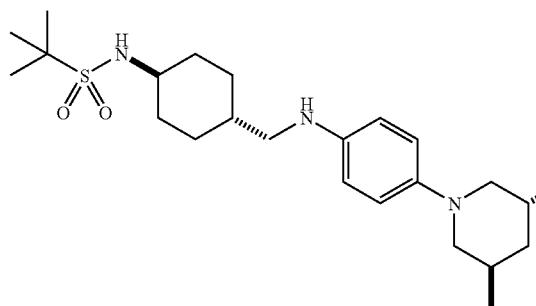


Ia-37



159

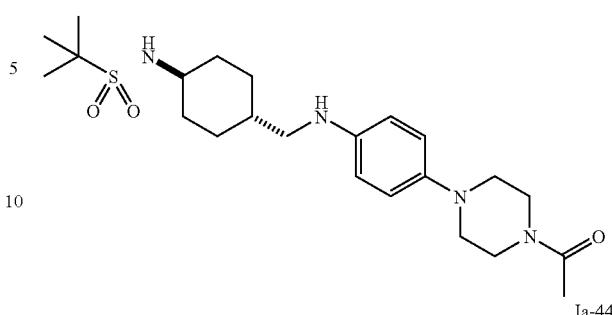
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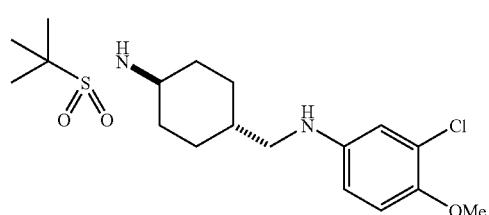
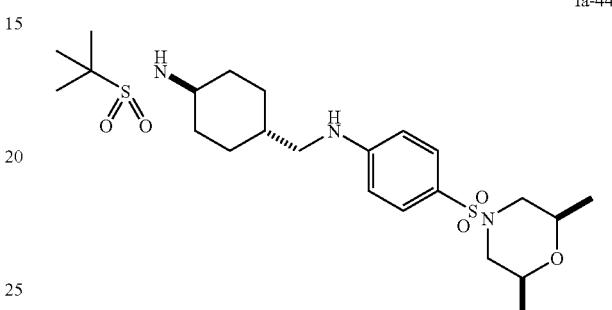
Ia-38

160

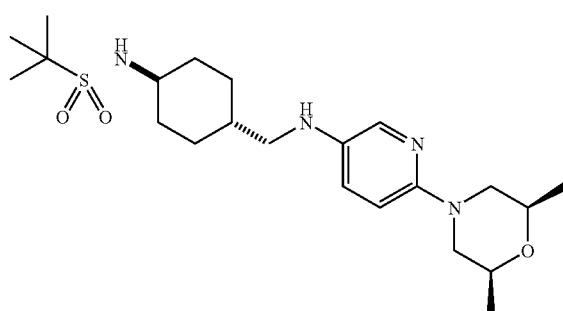
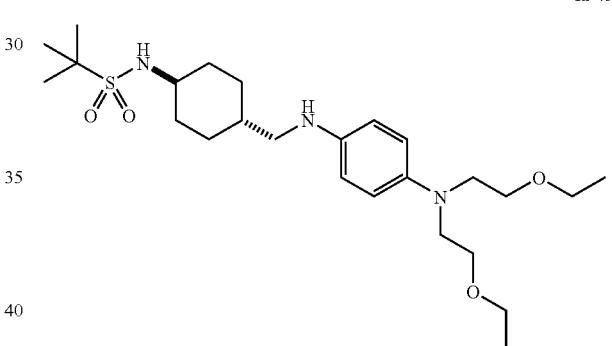
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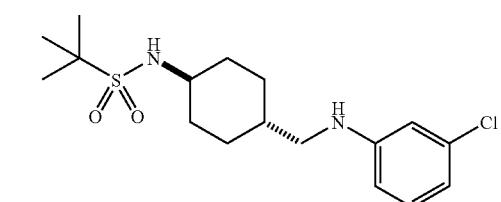
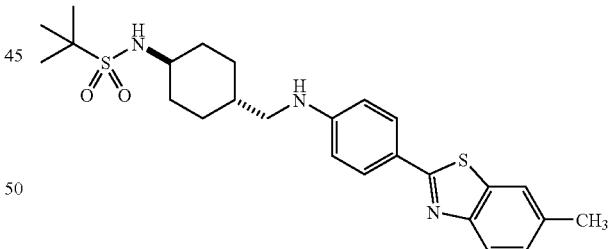
Ia-43

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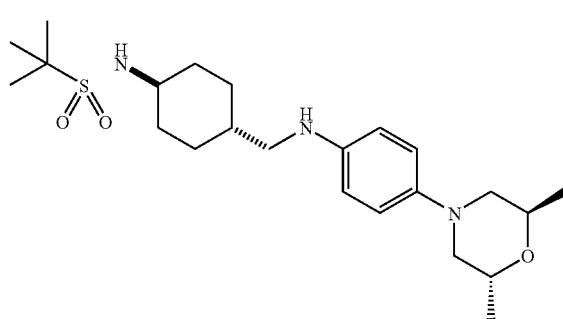
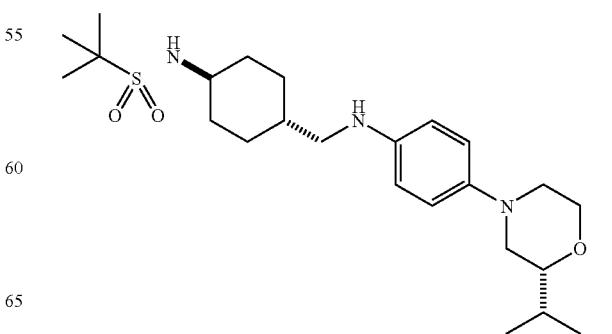
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Ia-46

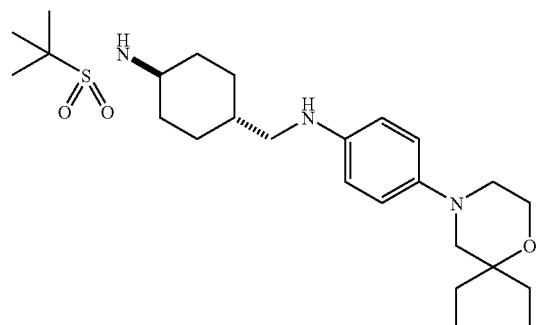
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Ia-47

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161

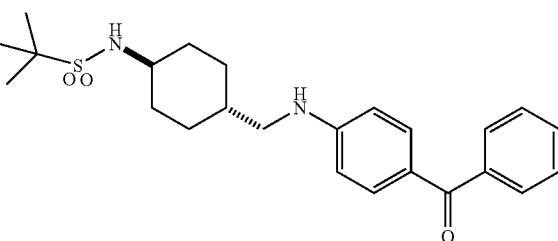
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Ia-48

162

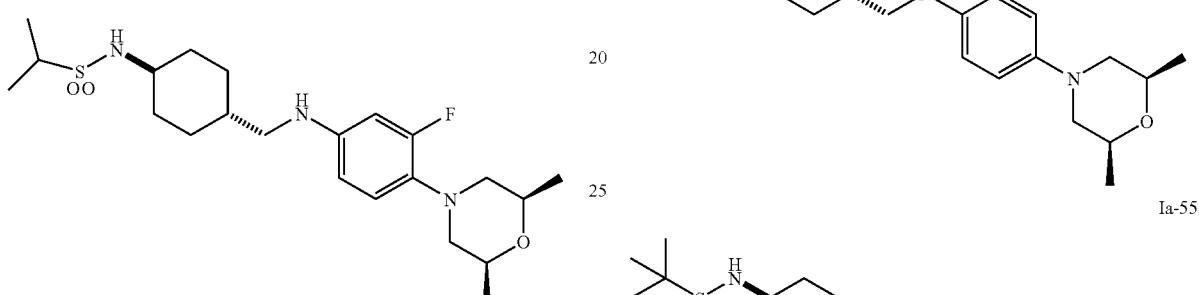
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Ia-53

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Ia-49



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Ia-50

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Ia-51

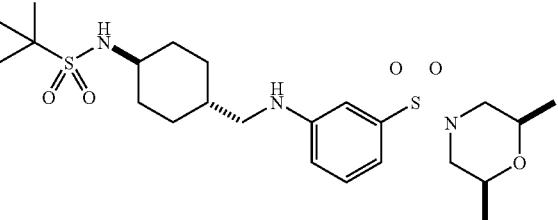
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Ia-52

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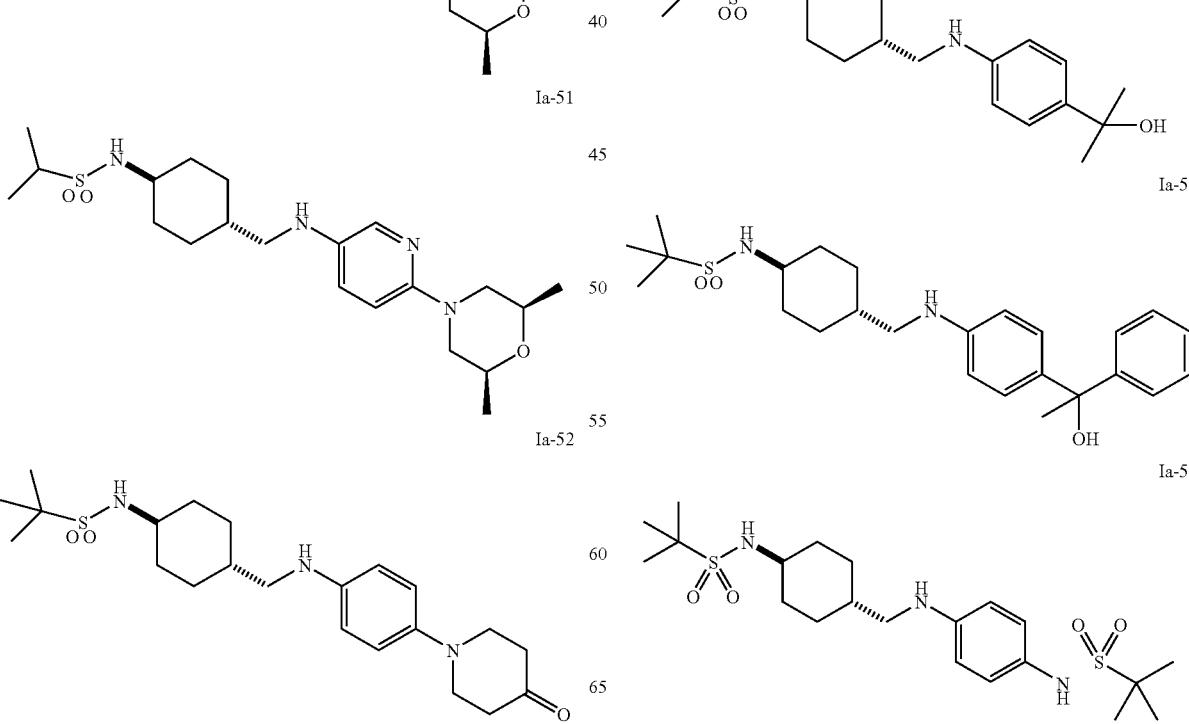
Ia-54

Ia-55

Ia-56

Ia-57

Ia-58



Ia-51

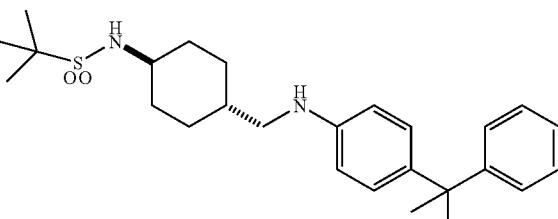
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Ia-52

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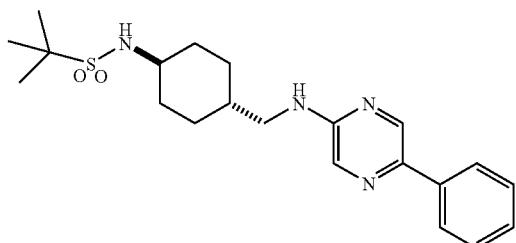


Ia-57

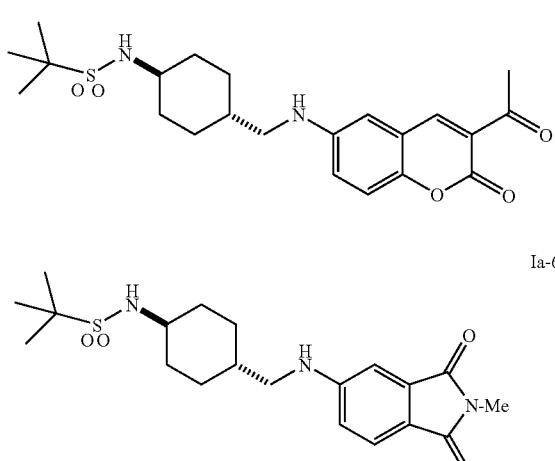
Ia-58

163

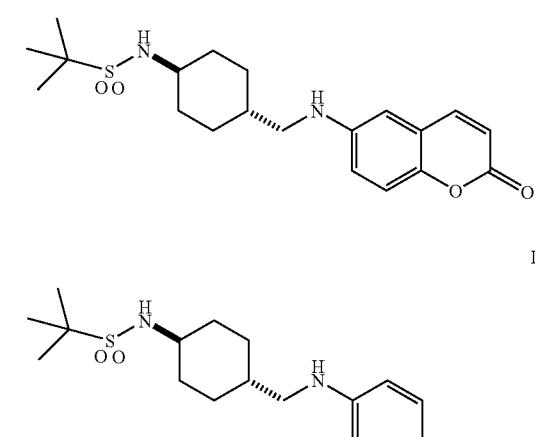
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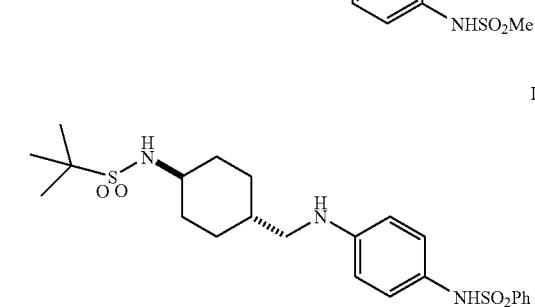
Ia-59



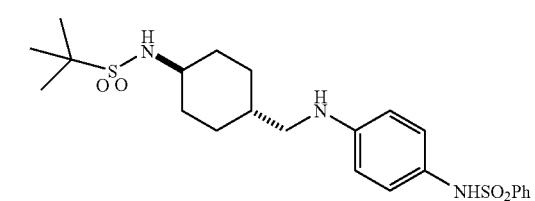
Ia-60



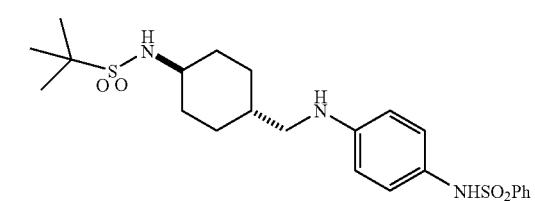
Ia-61



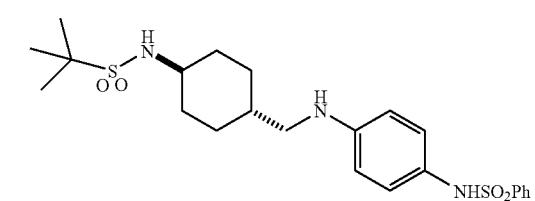
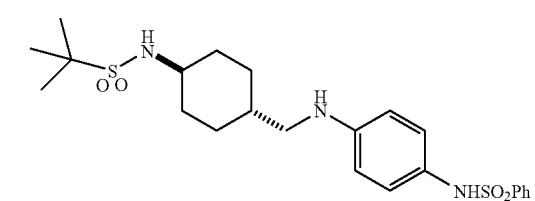
Ia-62



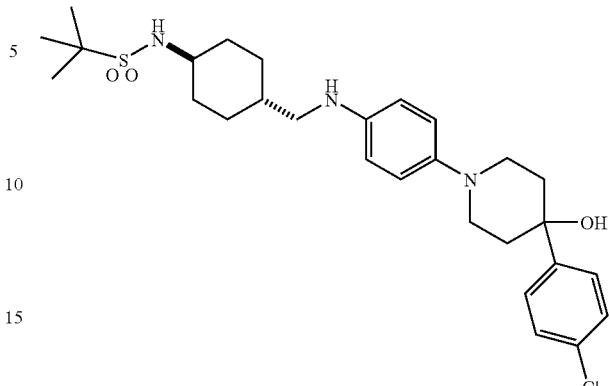
Ia-63



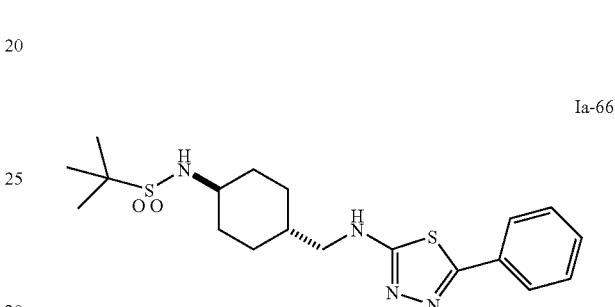
Ia-64

**164**

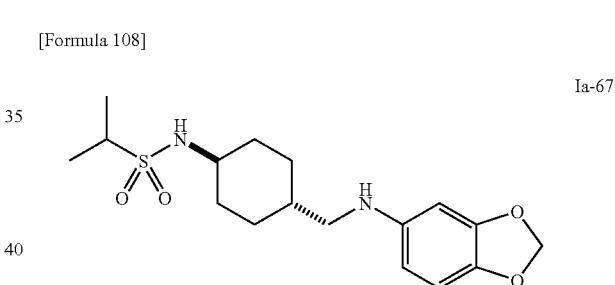
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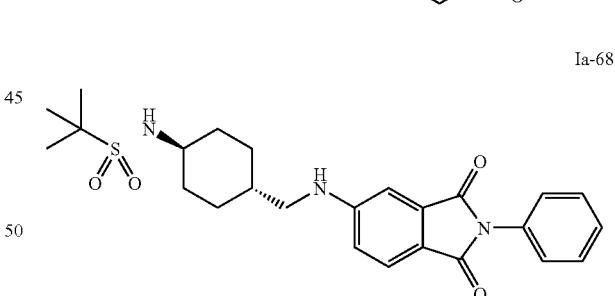
Ia-65



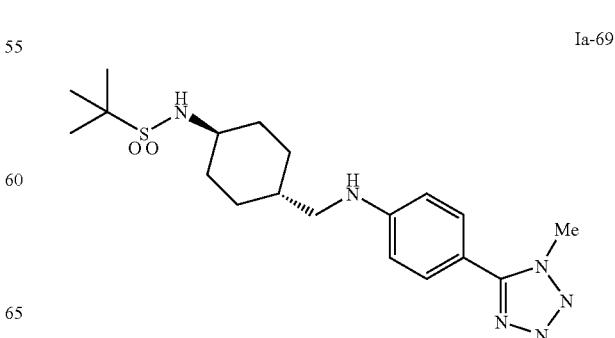
Ia-66



Ia-67



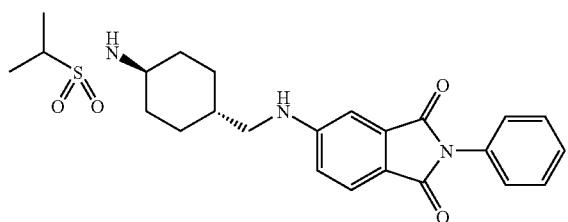
Ia-68



Ia-69

165

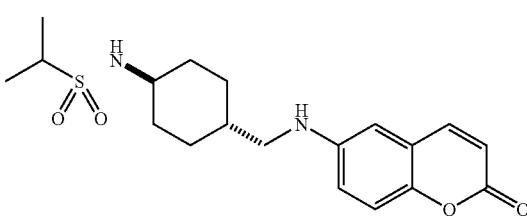
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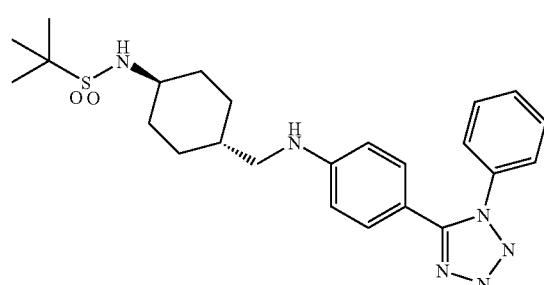
Ia-70

166

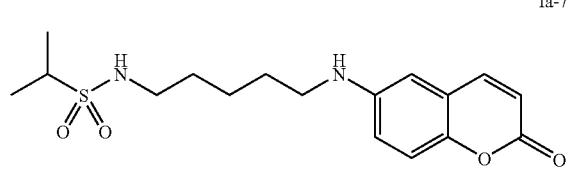
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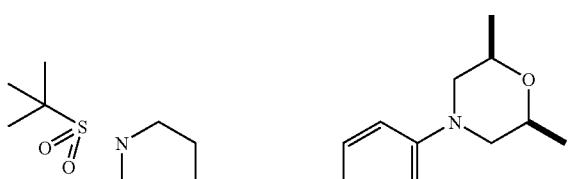
Ia-76



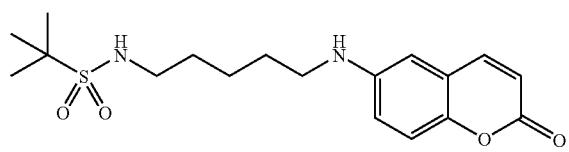
Ia-71



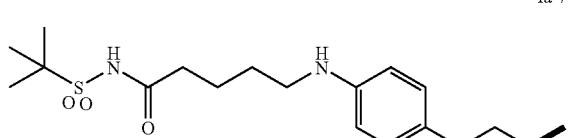
Ia-77



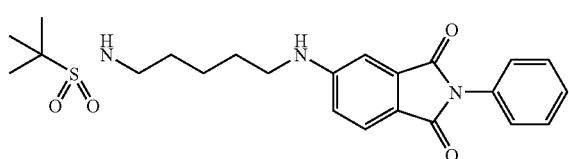
Ia-72



Ia-78



Ia-73



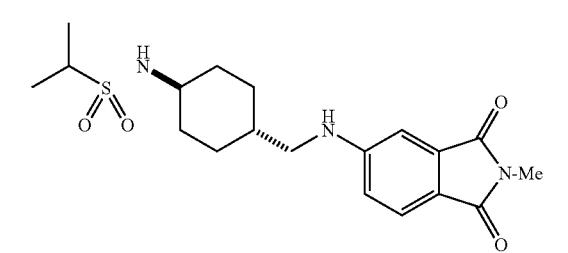
Ia-79



Ia-74

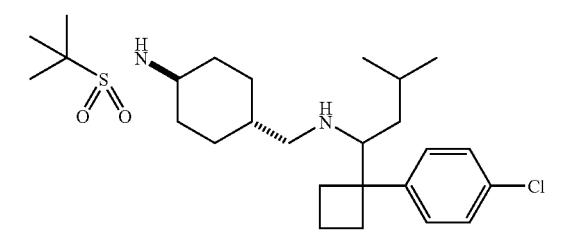


Ia-80

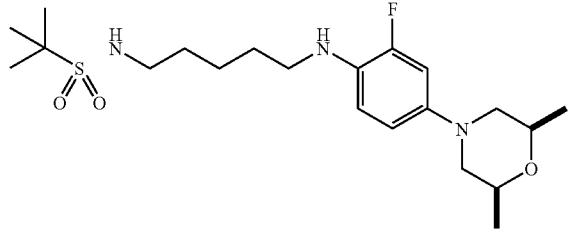


Ia-75

Ia-81



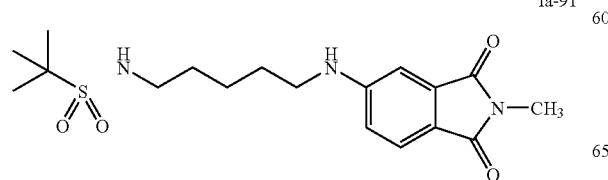
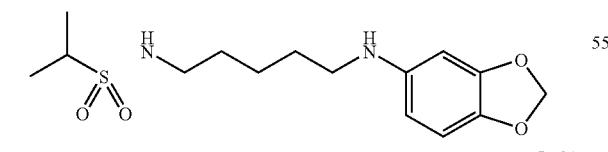
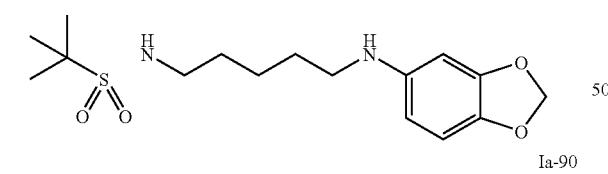
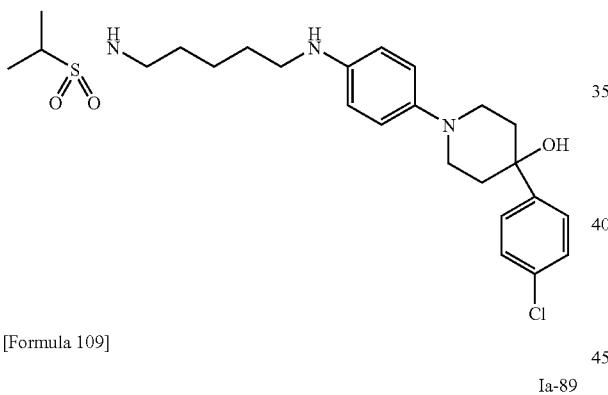
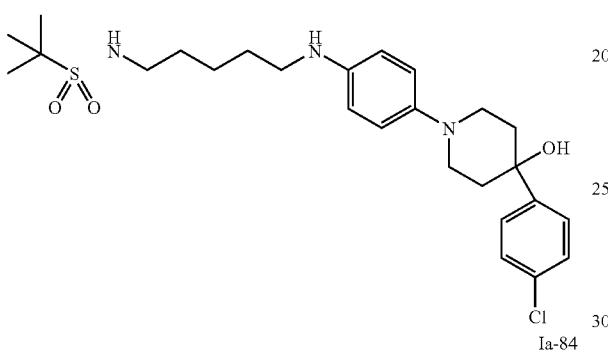
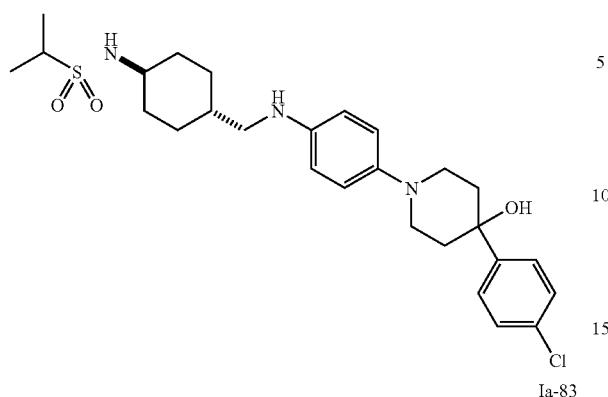
Ia-76



Ia-82

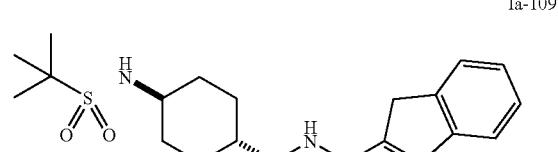
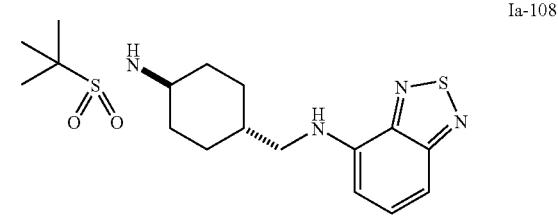
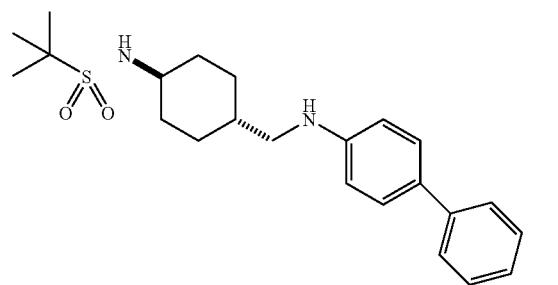
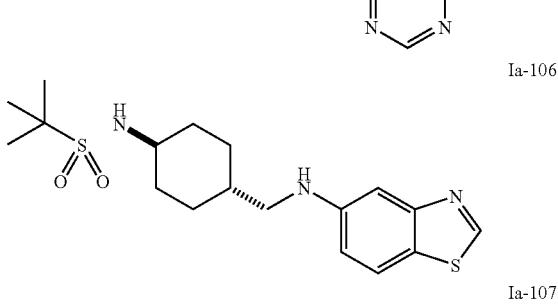
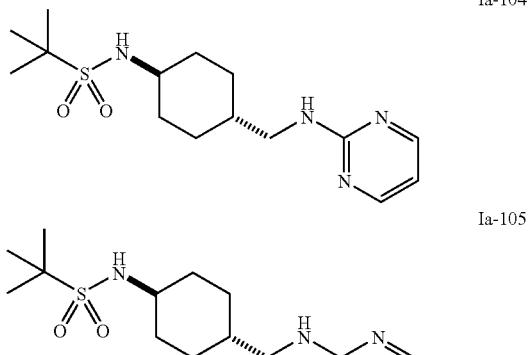
167

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**168**

-continued

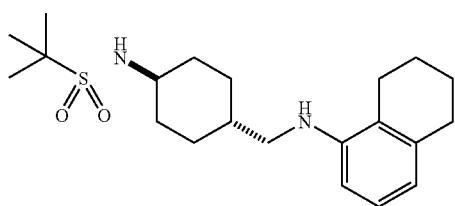
Ia-104



[Formula 109]

169

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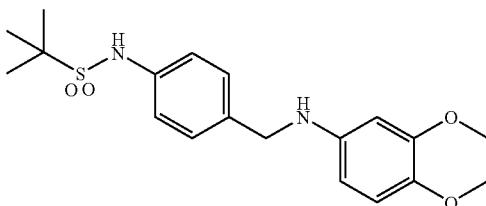


Ia-111

10

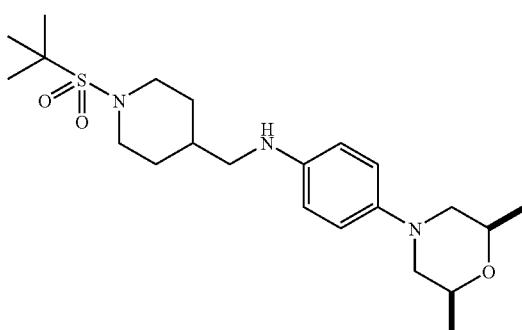
170

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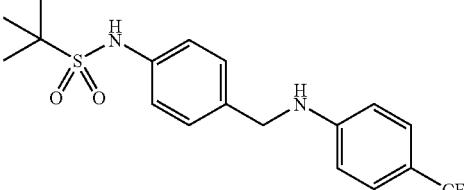


Ia-127

Ia-122

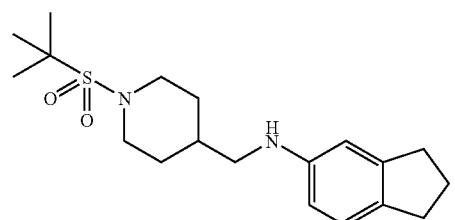


15

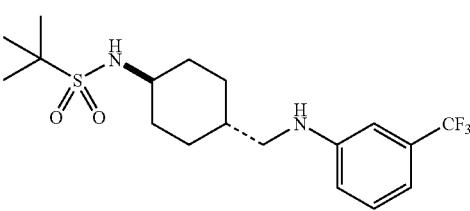


Ia-128

Ia-123

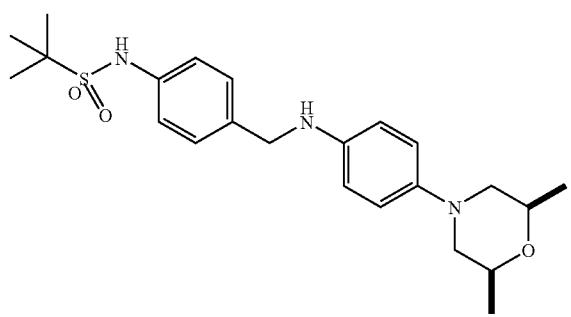


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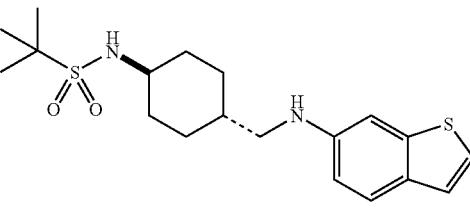


Ia-129

Ia-124

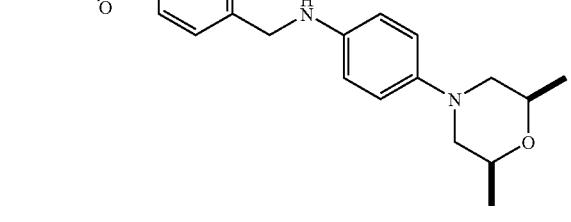


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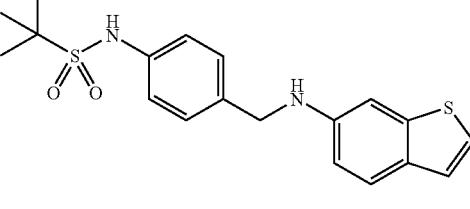


Ia-130

Ia-125

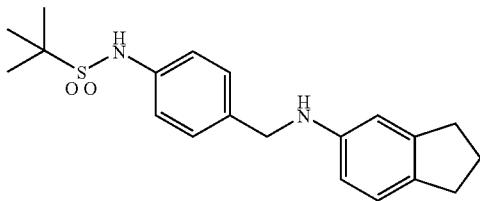


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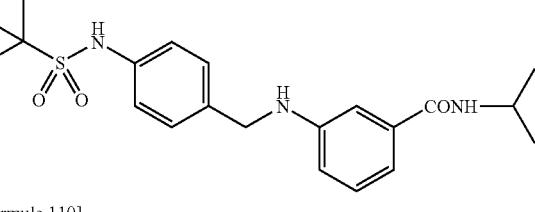


Ia-131

Ia-126

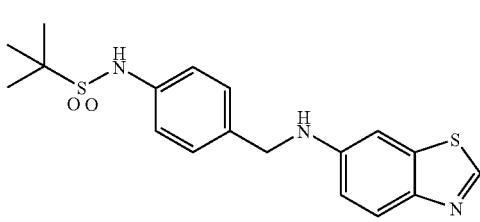


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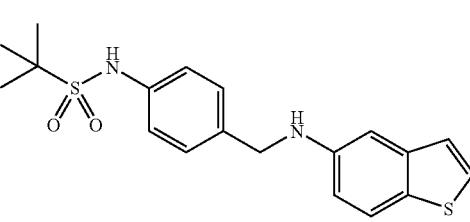


Ia-132

Ia-127



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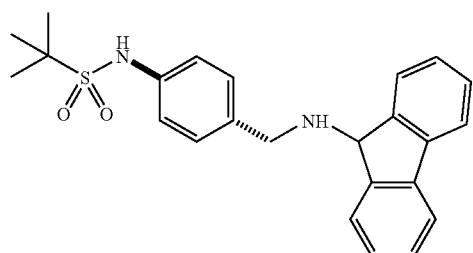
Ia-133

65

[Formula 110]

171

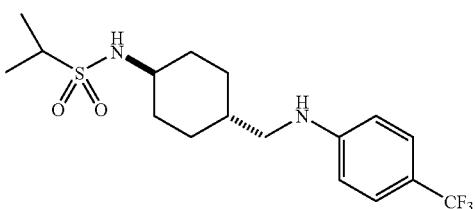
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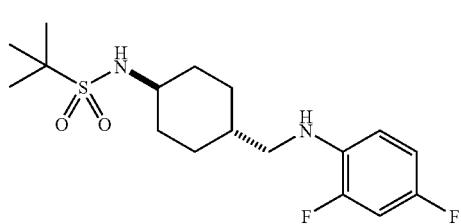
Ia-134

172

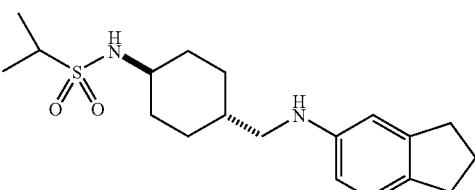
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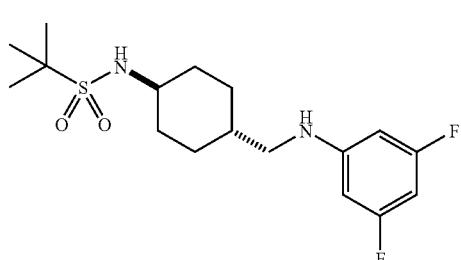
Ia-140



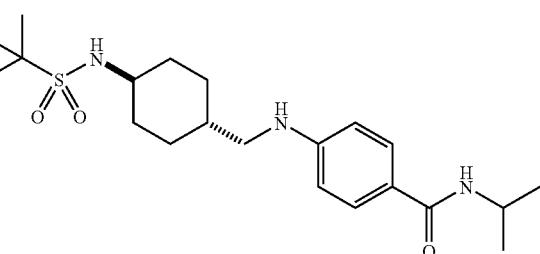
Ia-135



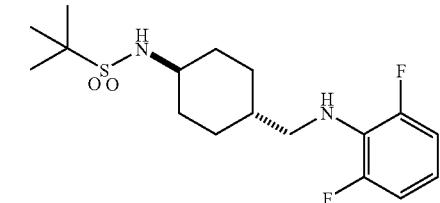
Ia-141



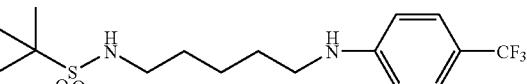
Ia-136



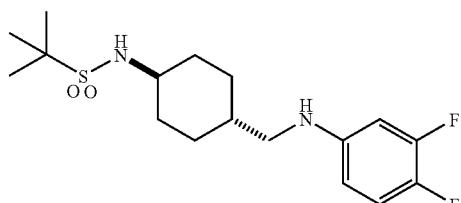
Ia-142



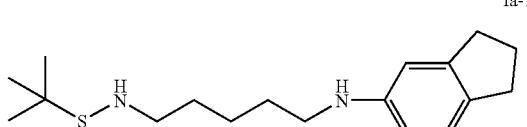
Ia-137



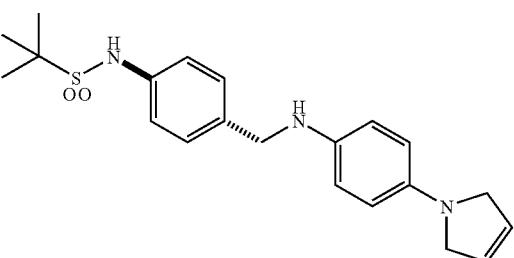
Ia-144



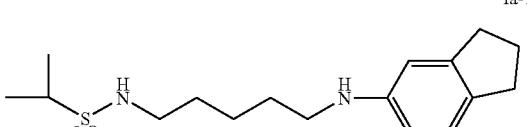
Ia-138



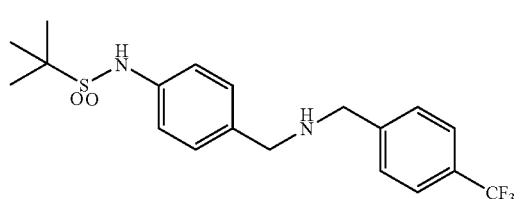
Ia-145



Ia-139



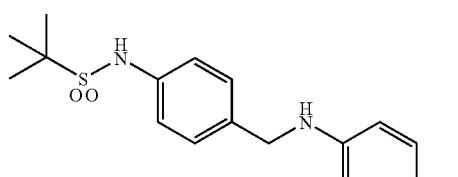
Ia-146



Ia-147

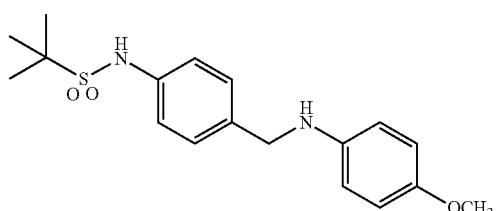
173

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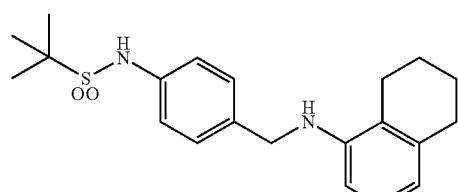


Ia-148

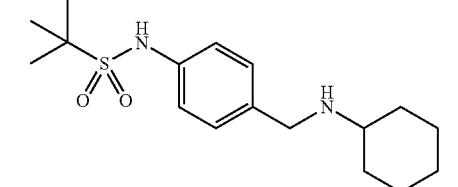
[Formula 111]



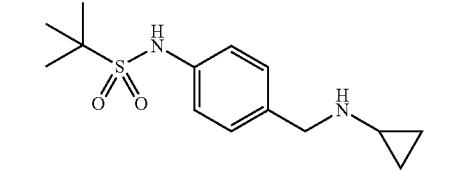
Ia-149



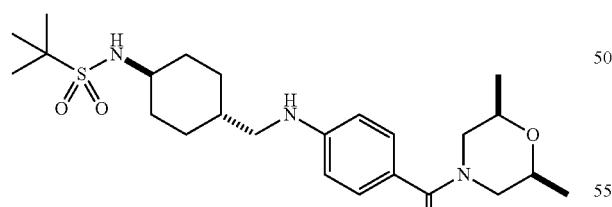
Ia-150



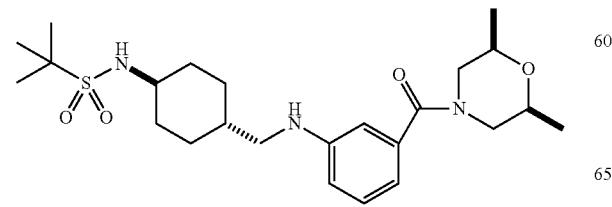
Ia-151



Ia-152



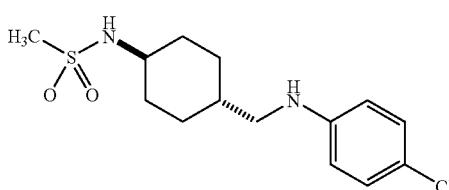
Ia-153



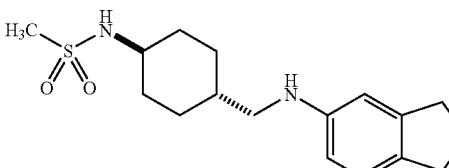
Ia-154

174

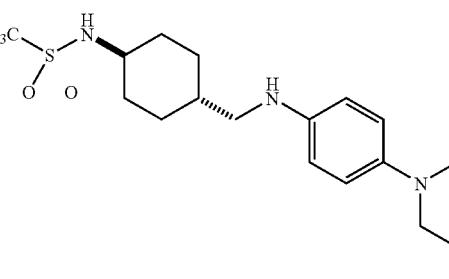
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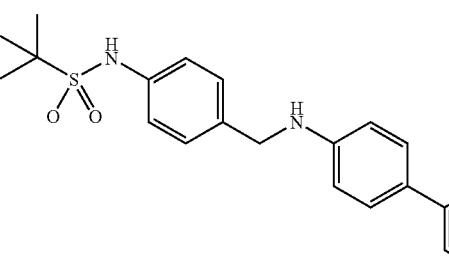
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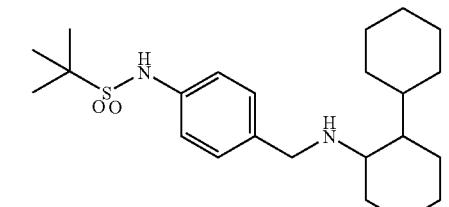
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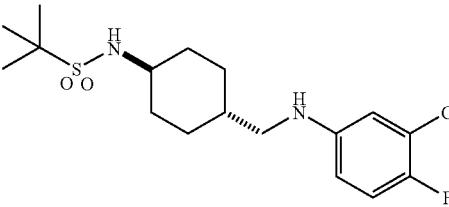
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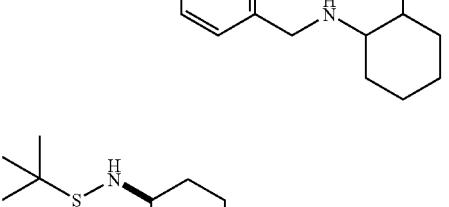
35



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Ia-155

Ia-156

Ia-157

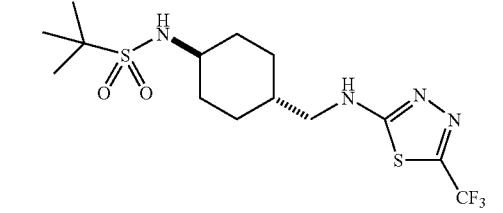
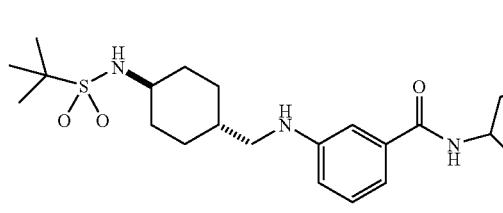
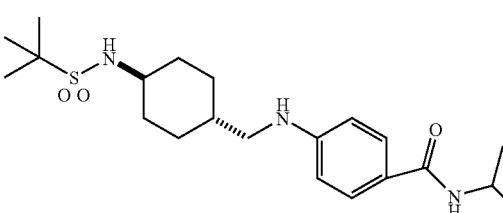
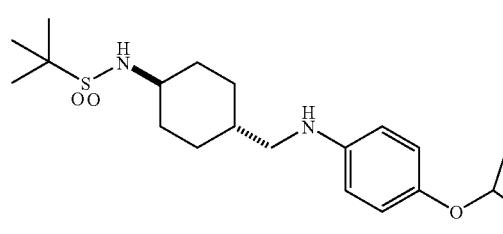
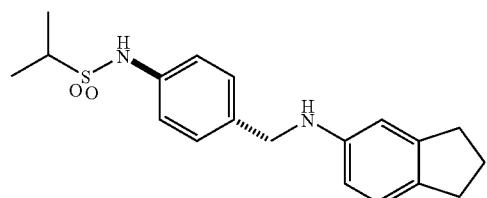
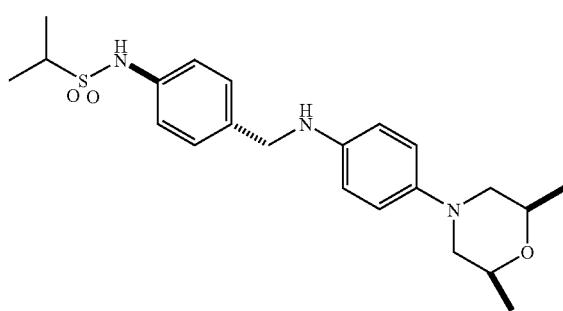
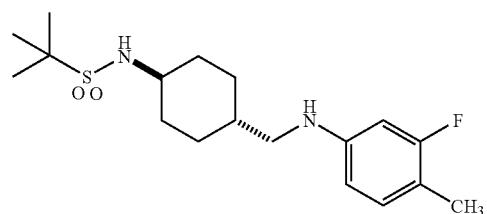
Ia-158

Ia-159

Ia-160

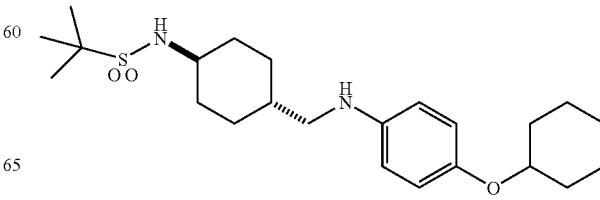
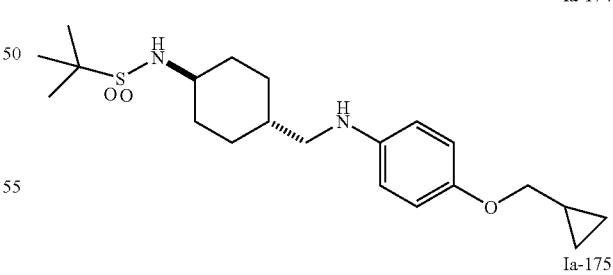
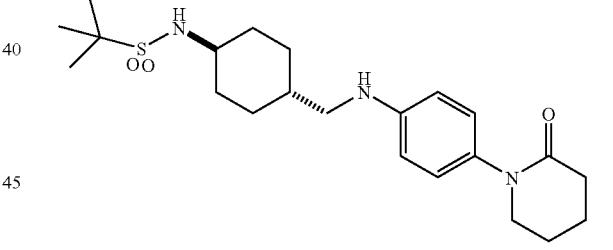
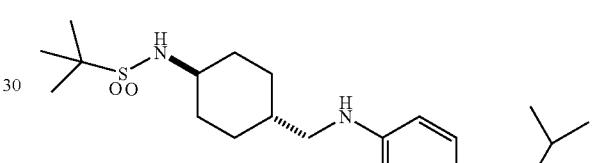
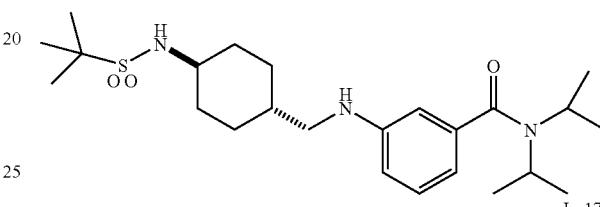
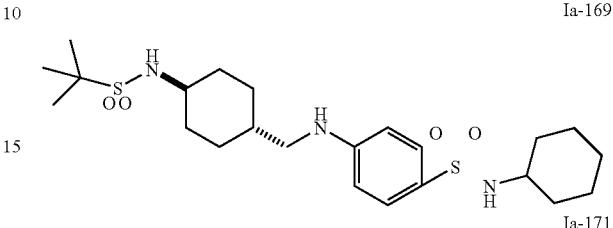
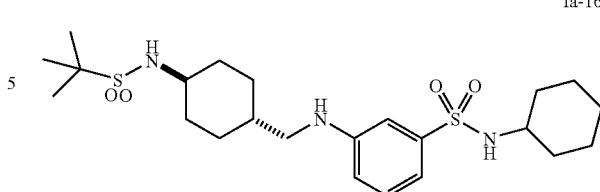
175

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**176**

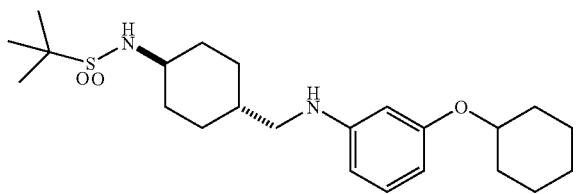
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Ia-168

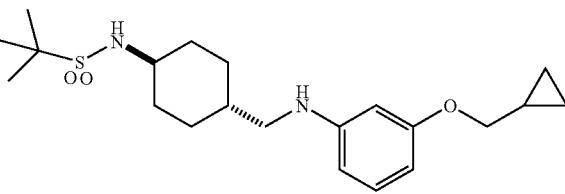


177

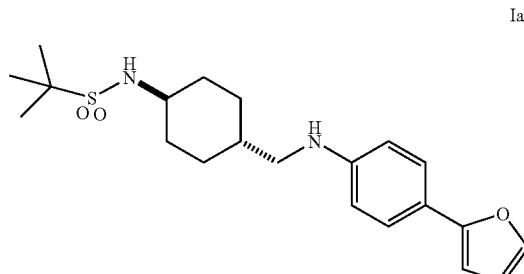
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5
10**178**

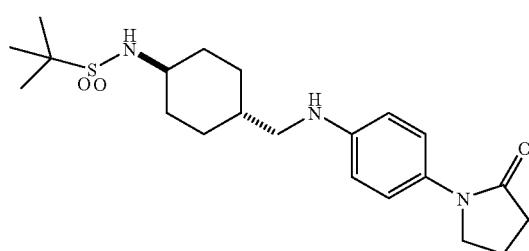
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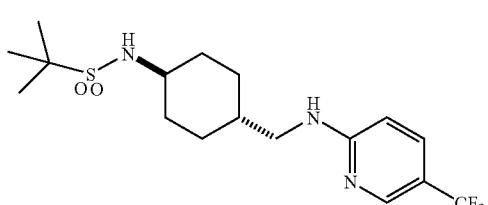
[Formula 112]



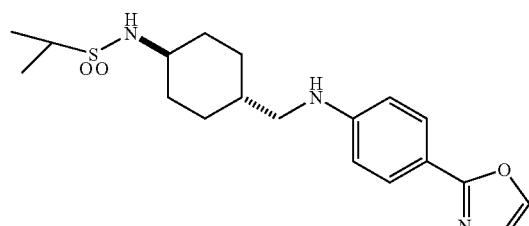
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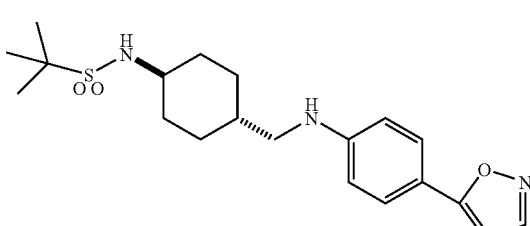
25



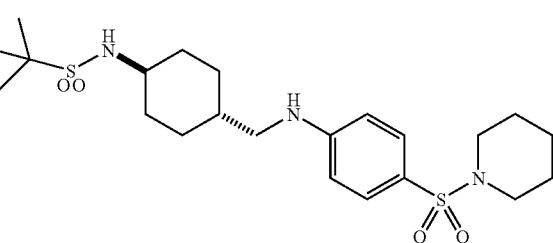
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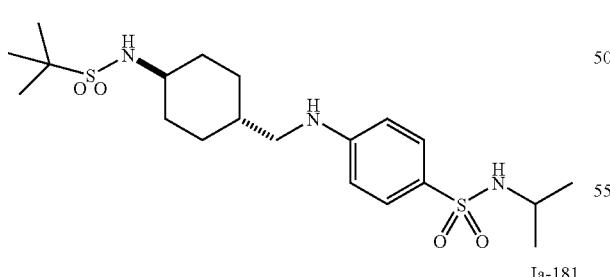
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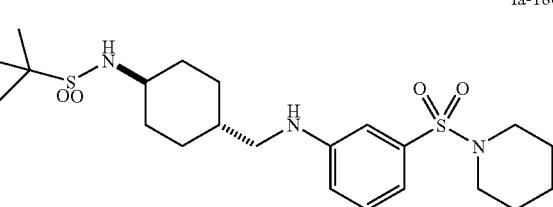
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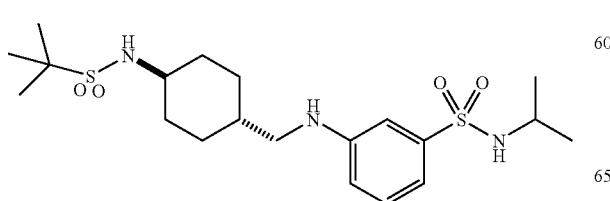
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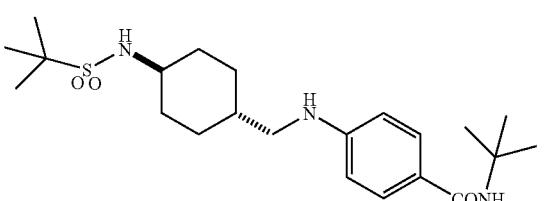
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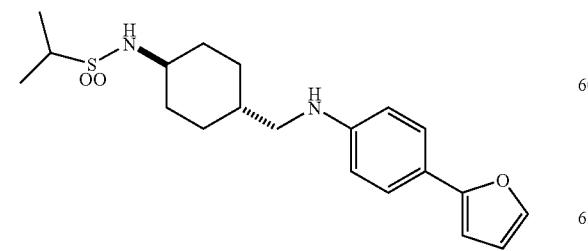
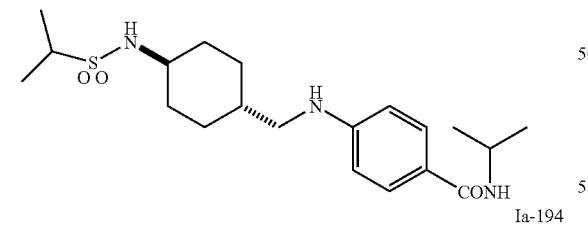
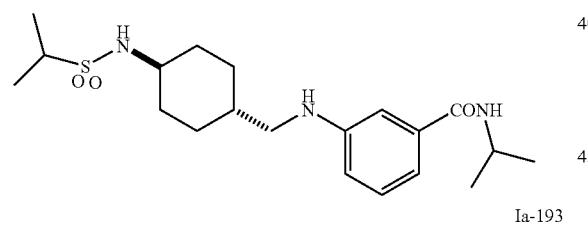
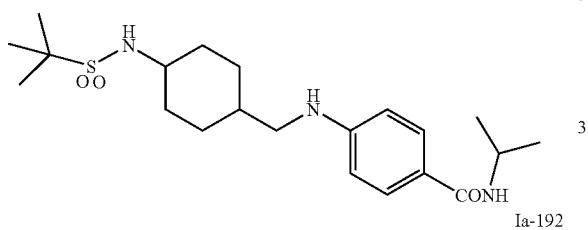
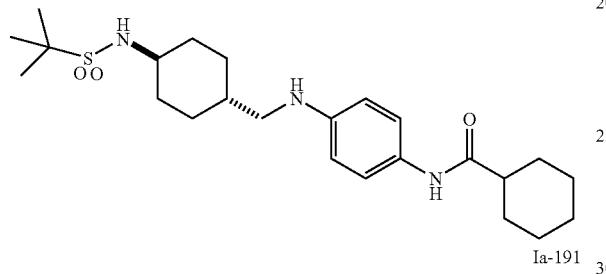
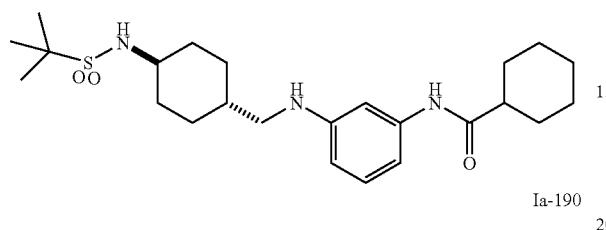
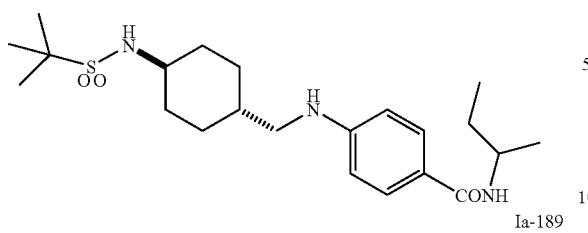


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179

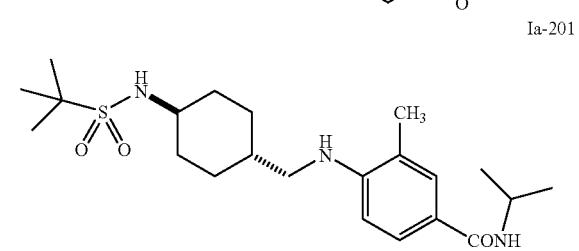
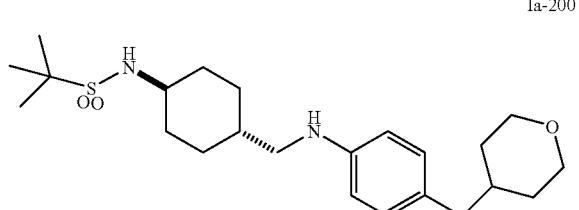
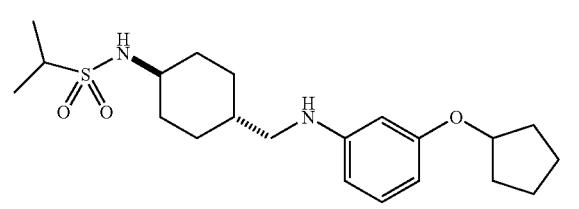
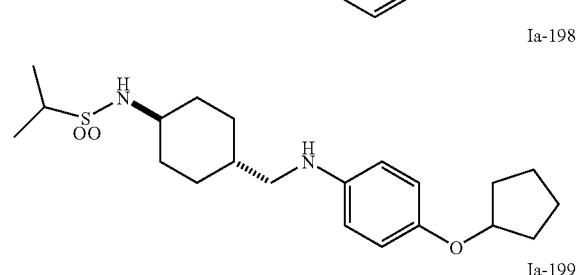
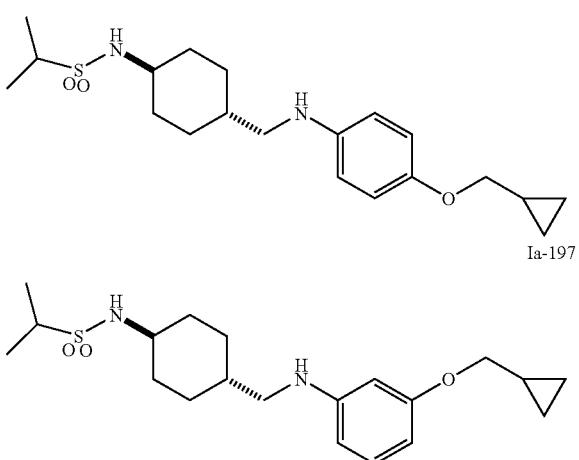
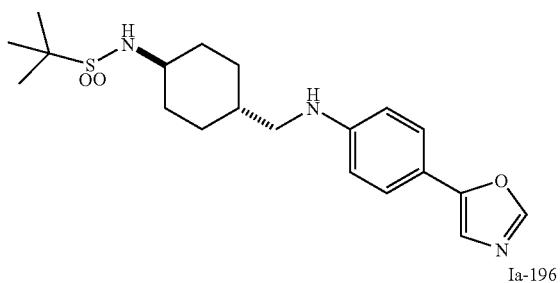
-continued

Ia-188

**180**

-continued

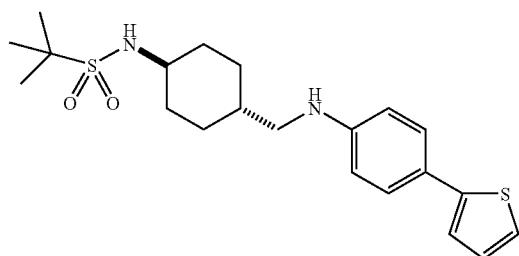
Ia-195



181

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Ia-202

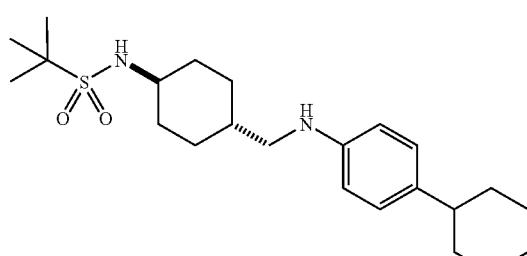


[Formula 113]

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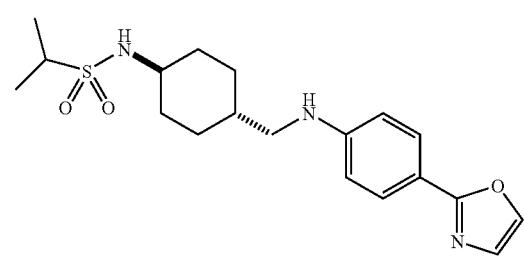
10

Ia-203 15



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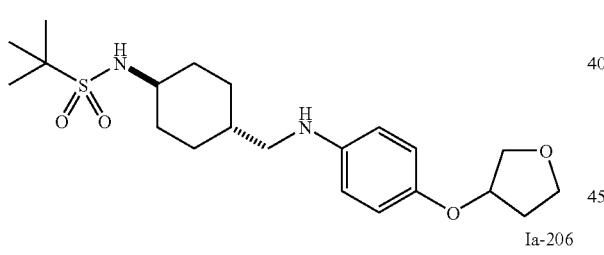
Ia-204



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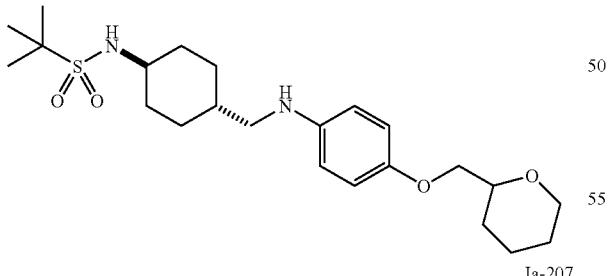
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Ia-205



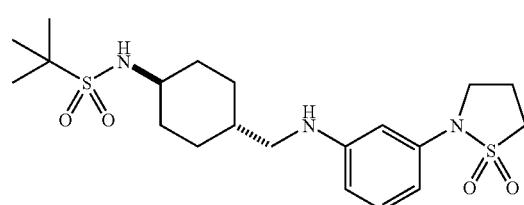
40

Ia-206



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Ia-207



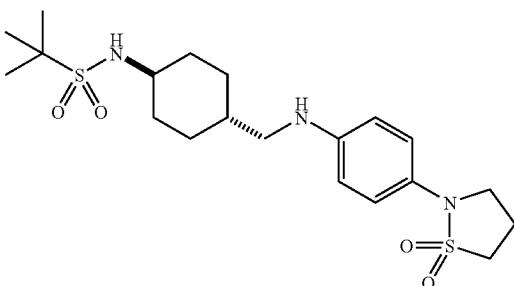
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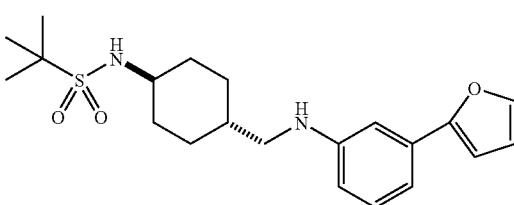
182

-continued

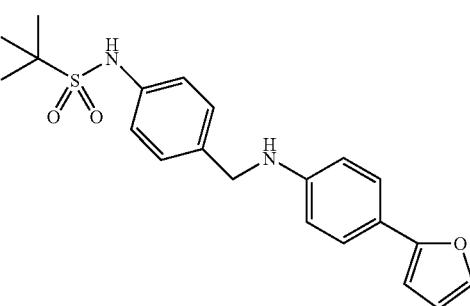
Ia-208



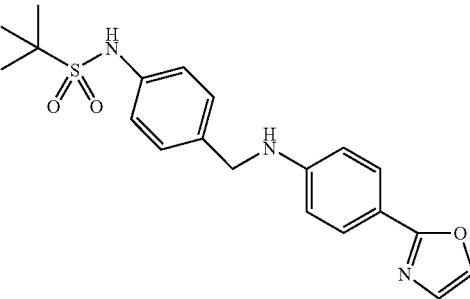
Ia-209



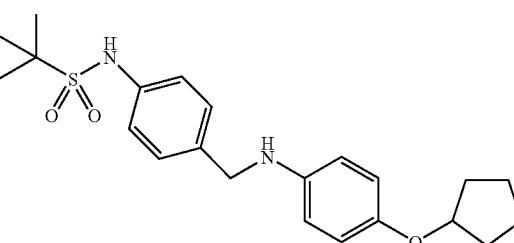
Ia-210



Ia-211

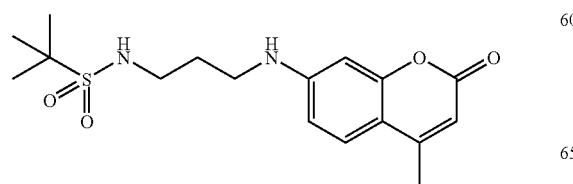
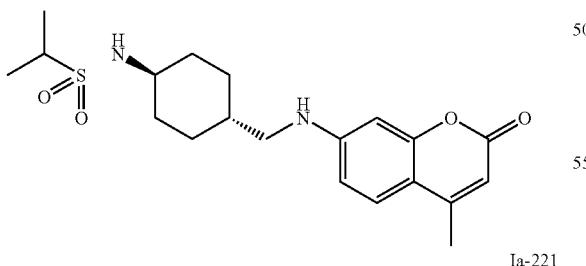
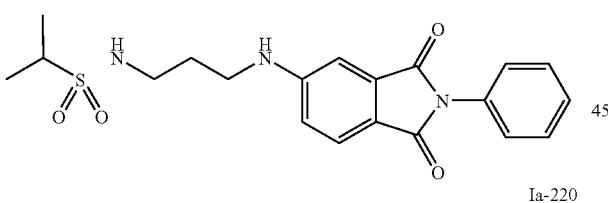
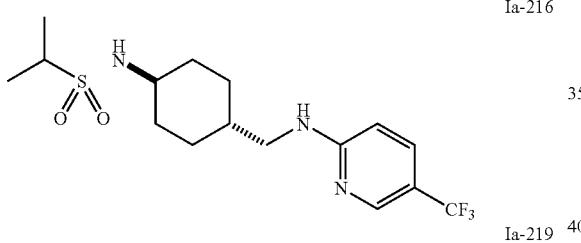
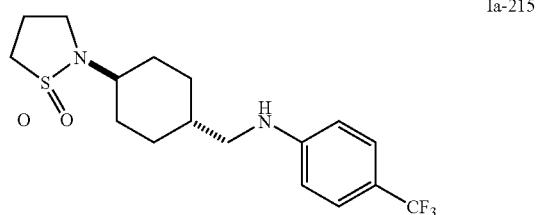
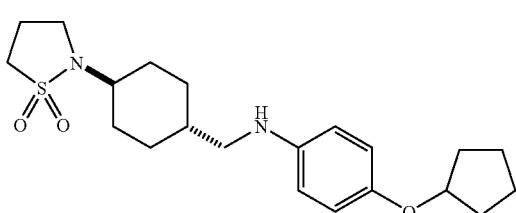
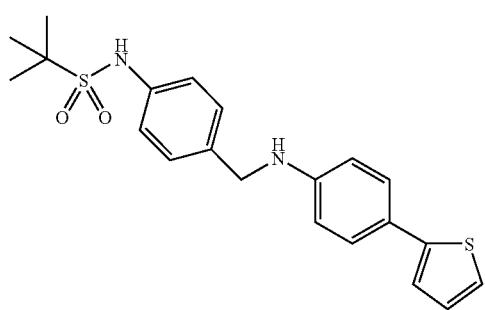


Ia-212



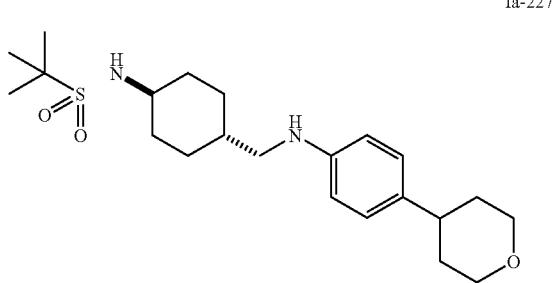
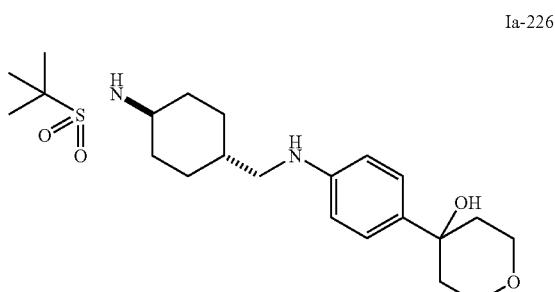
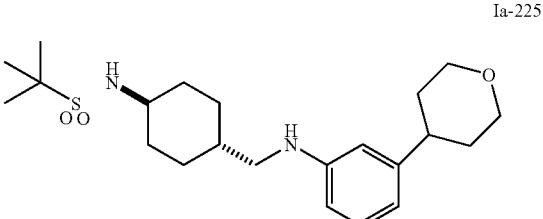
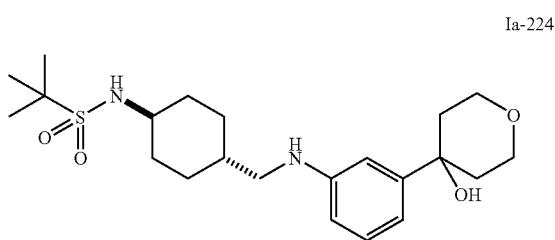
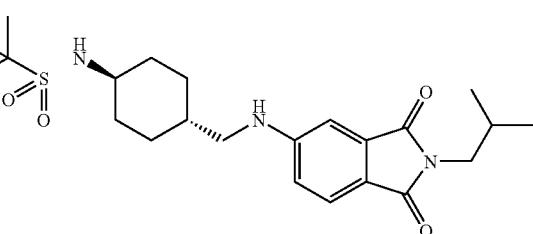
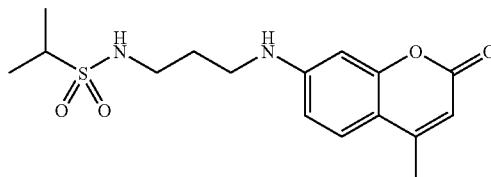
183

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**184**

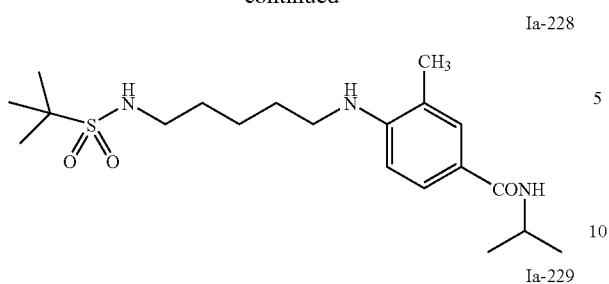
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Ia-222



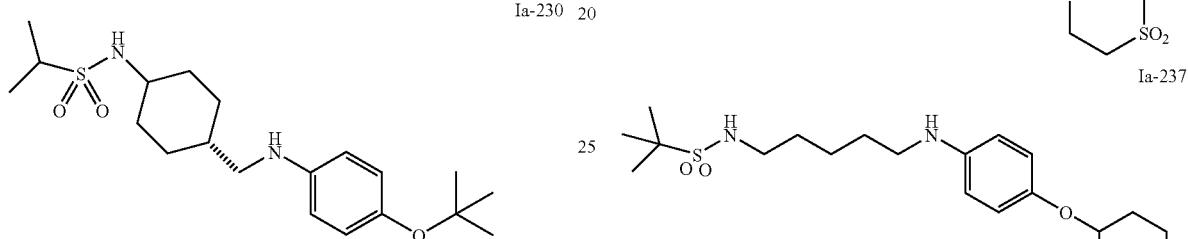
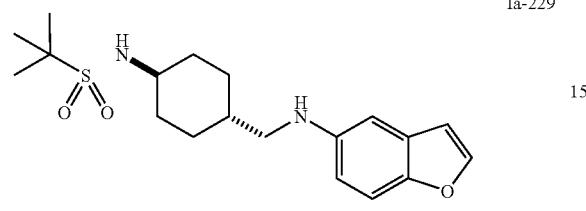
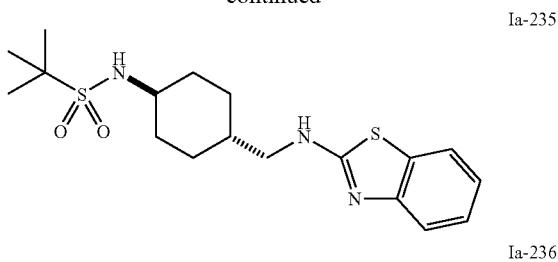
185

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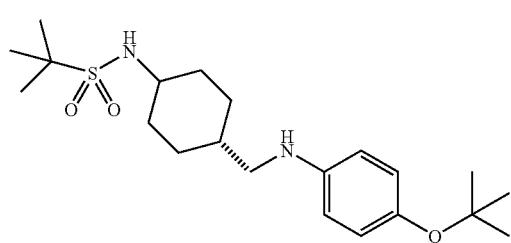
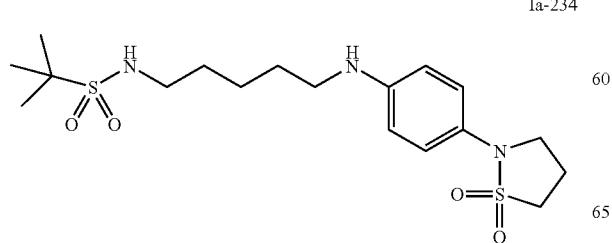
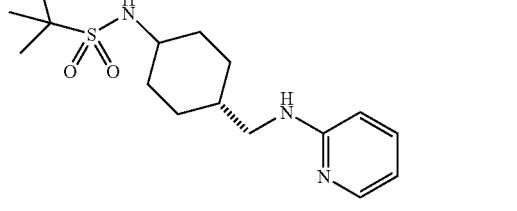
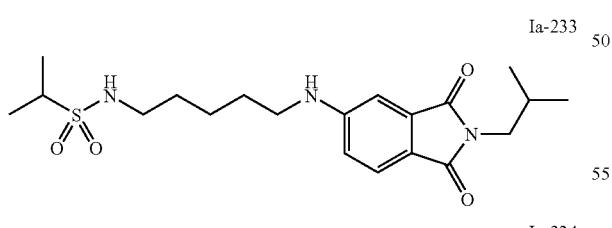
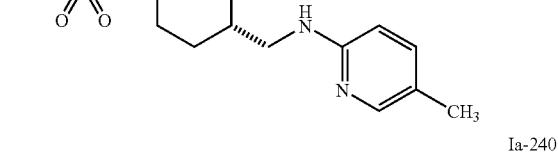
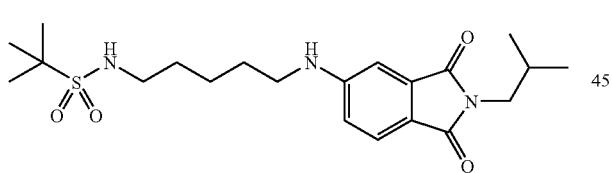
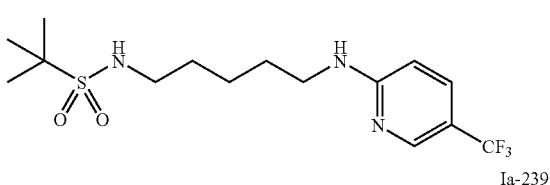
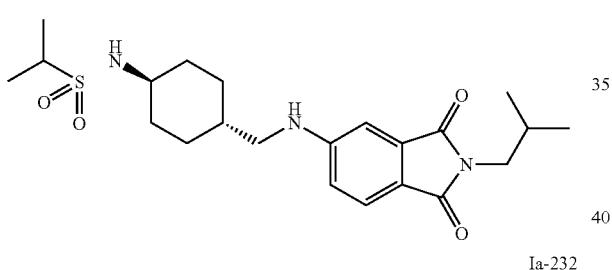


186

-continued

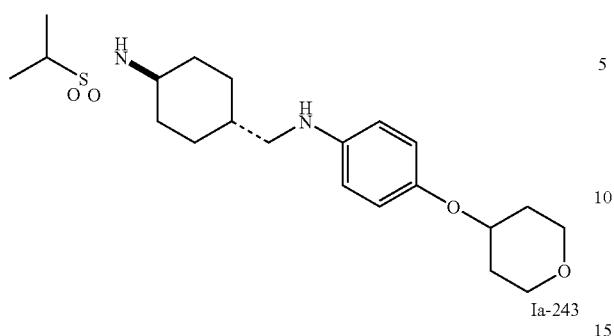


[Formula 114]



187
-continued

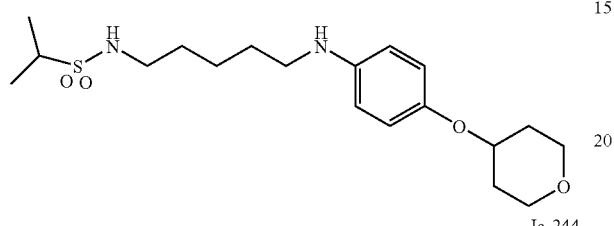
Ia-242



5

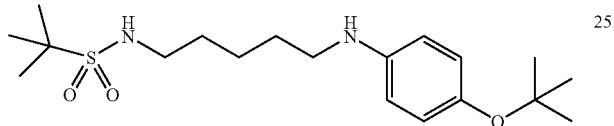
10

15



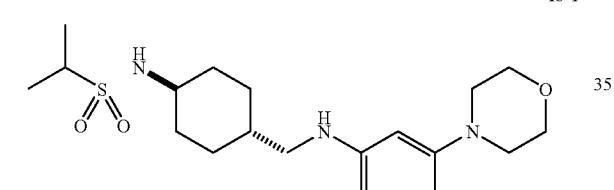
20

25

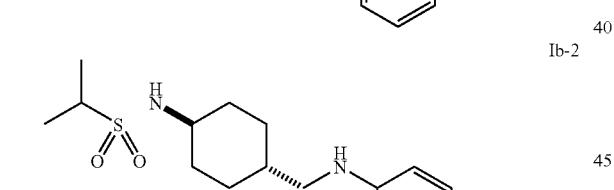


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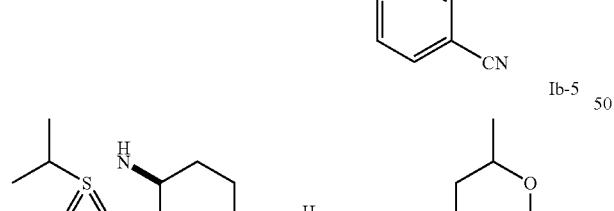
[Formula 115]



35

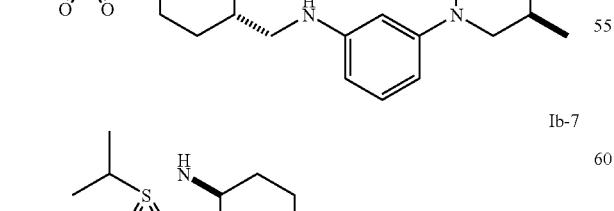


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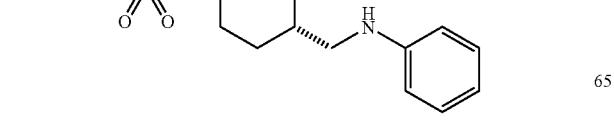
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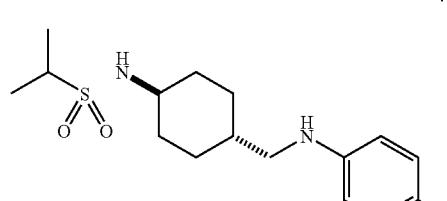
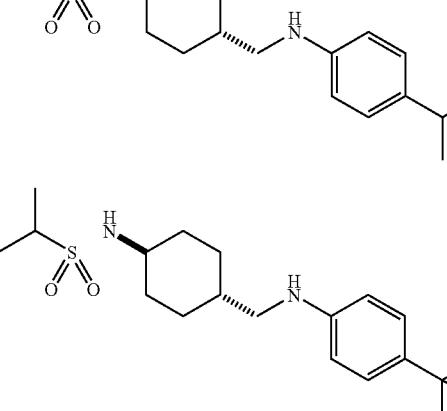
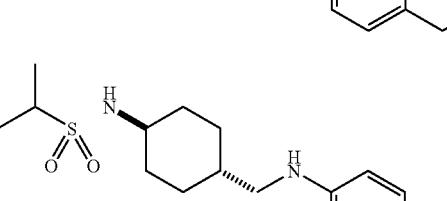
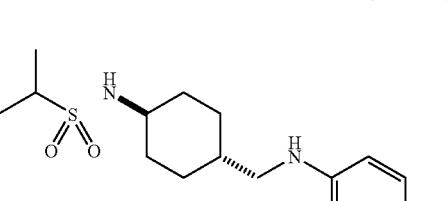
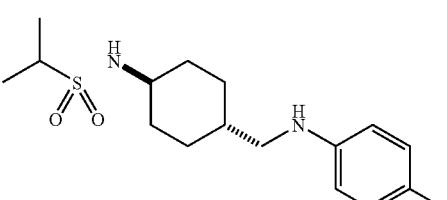
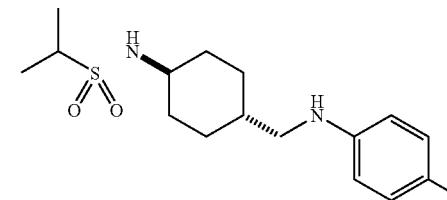
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65

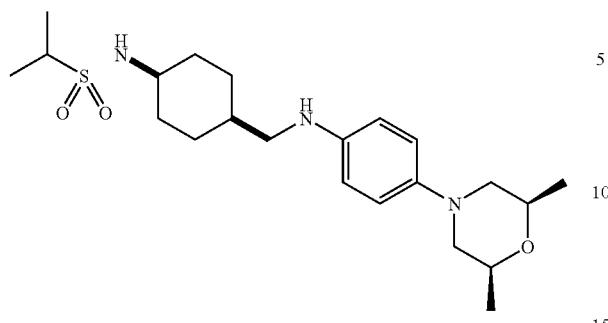
188
-continued

Ib-8

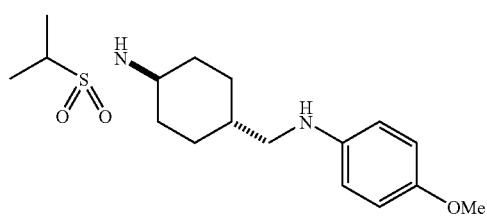


189

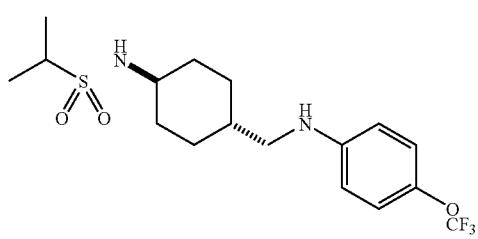
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Ib-16

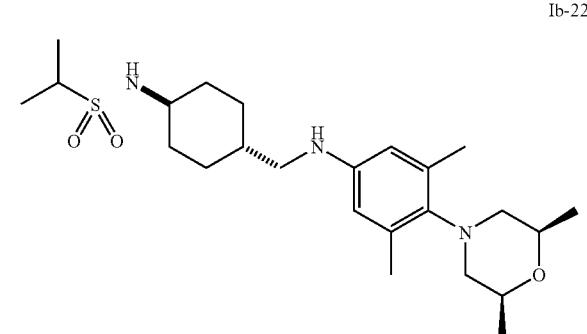


Ib-17



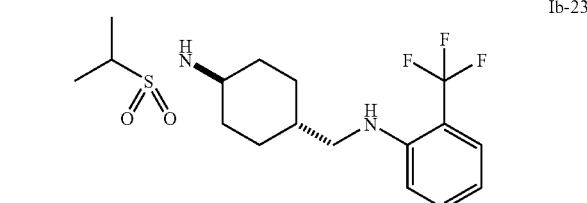
Ib-18

40



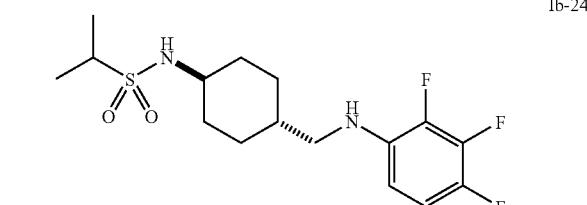
Ib-19

50



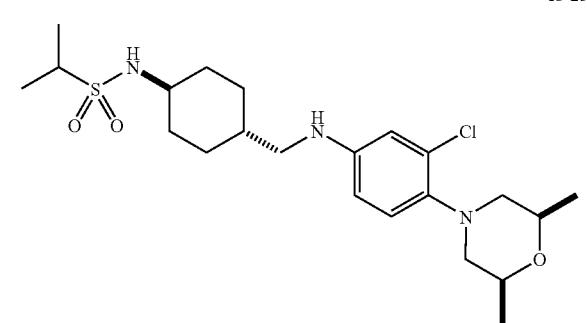
Ib-20

55



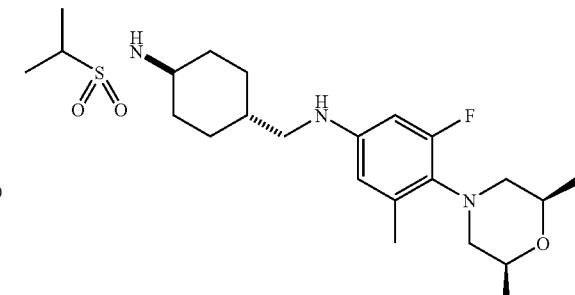
Ib-21

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**190**

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Ib-21



Ib-16

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Ib-17

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Ib-19

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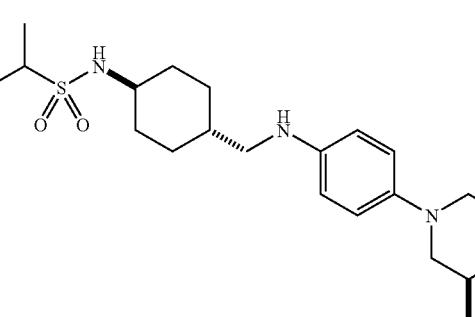
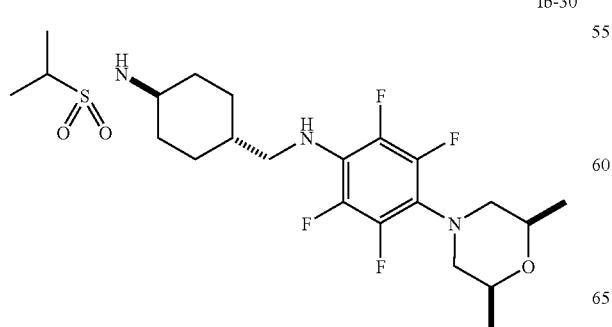
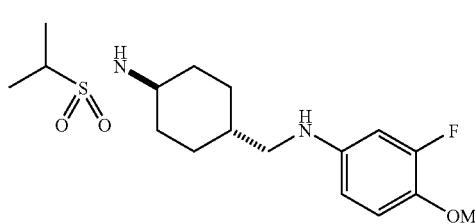
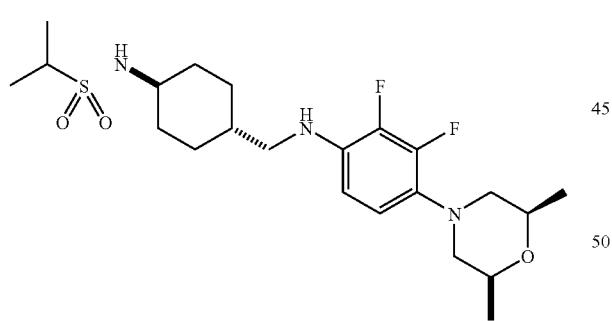
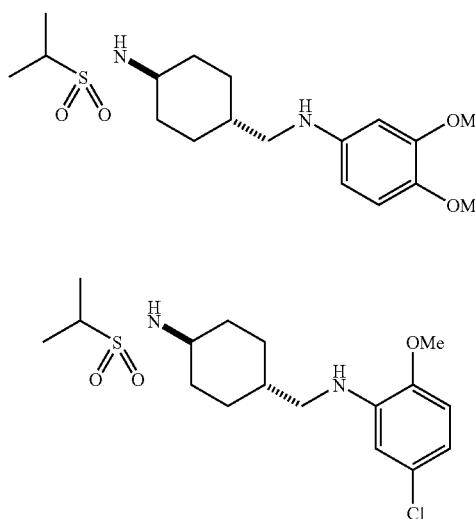
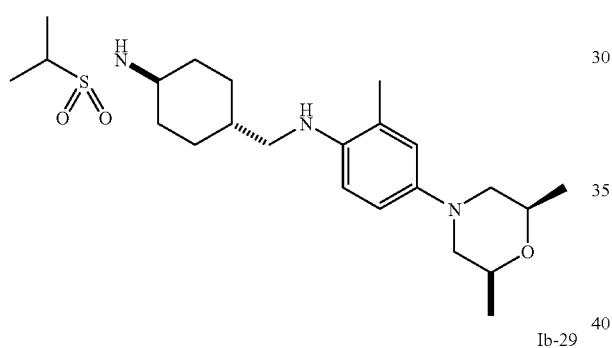
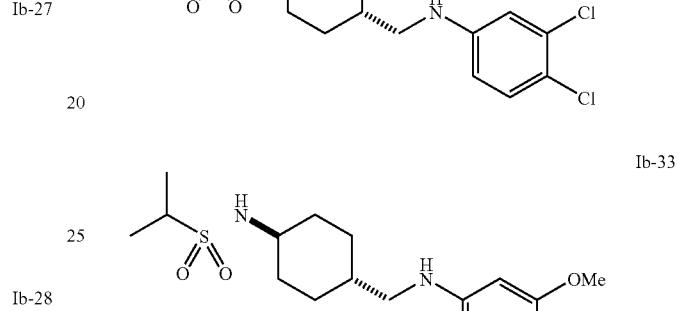
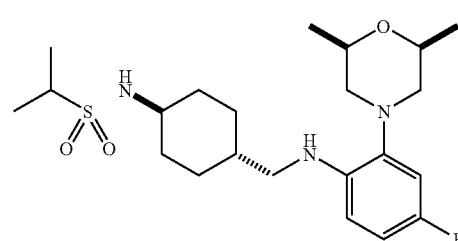
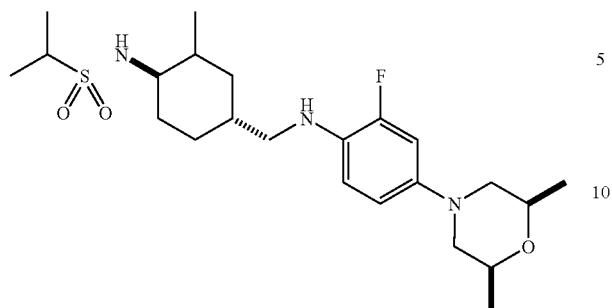
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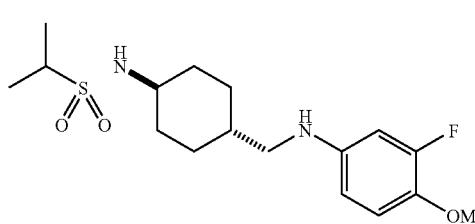
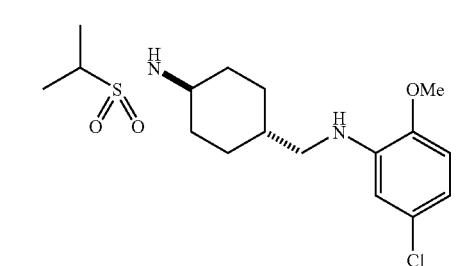
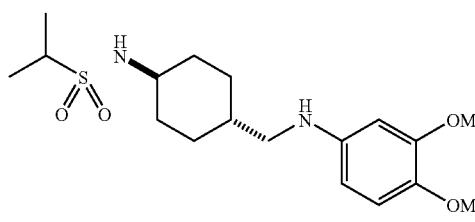
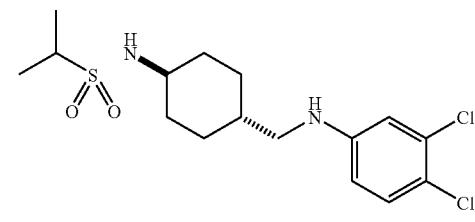
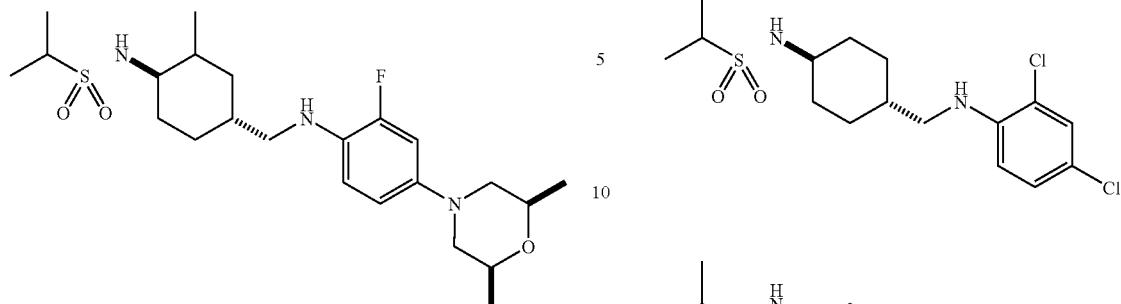
191

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**192**

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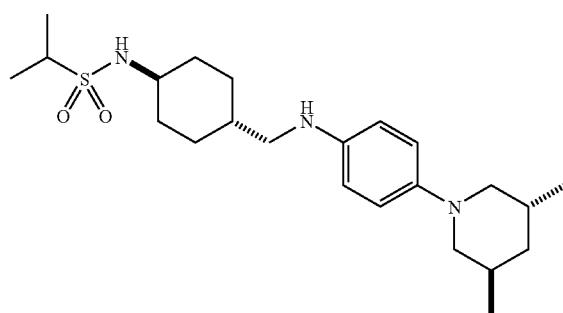
Ib-31



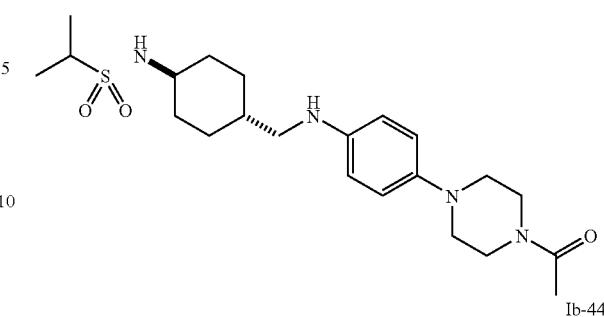
Ib-37

193

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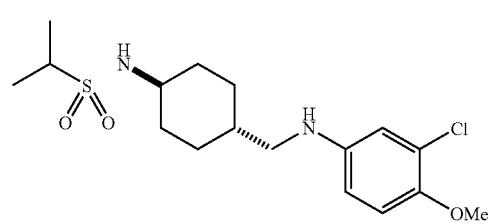


Ib-38

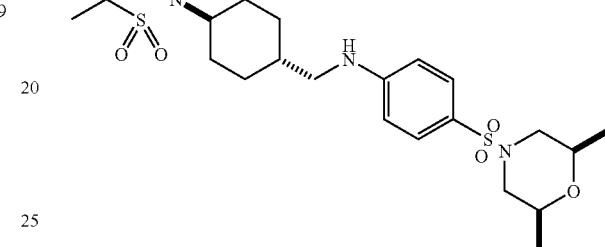
**194**

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Ib-43



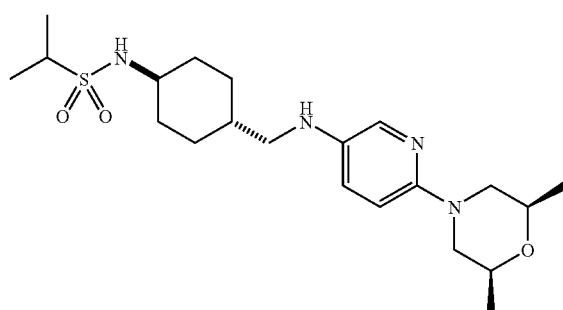
Ib-39



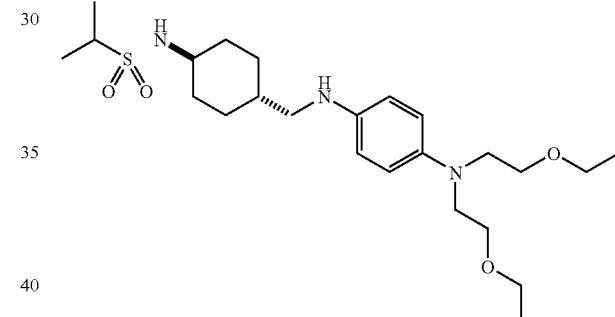
Ib-40

[Formula 117]

Ib-45

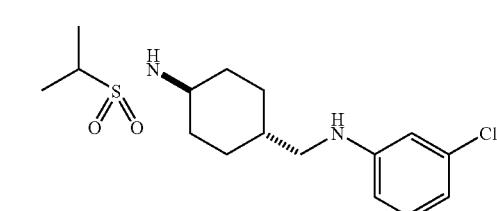


Ib-41



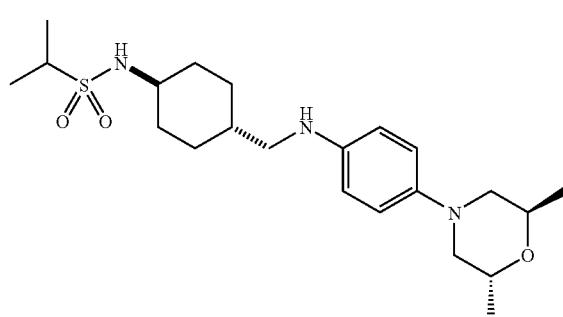
Ib-42

Ib-46



Ib-45

Ib-47



Ib-44

Ib-48

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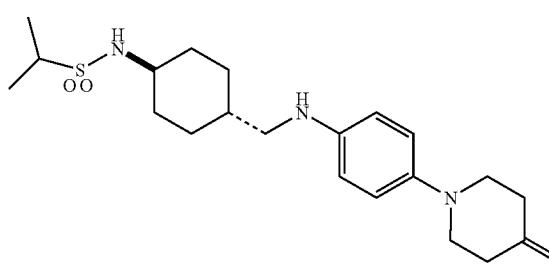
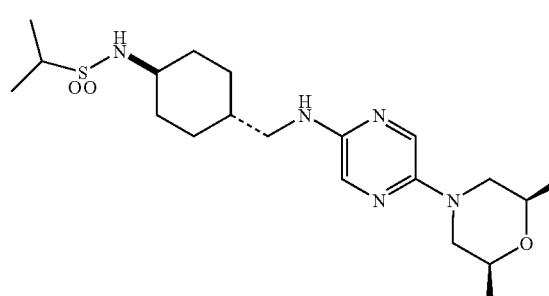
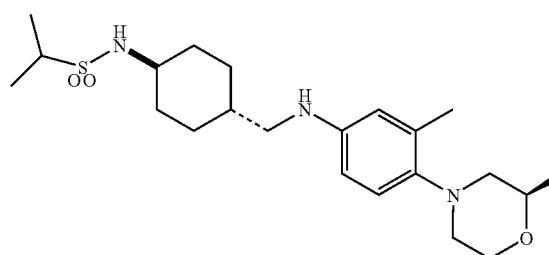
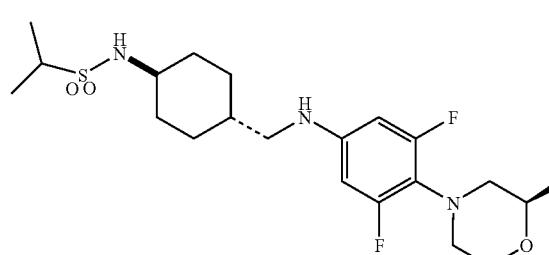
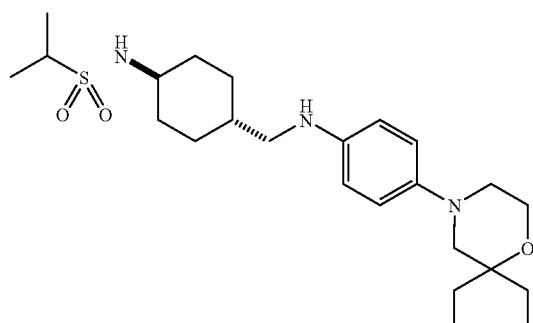
Ib-283

Ib-285

Ib-287

195

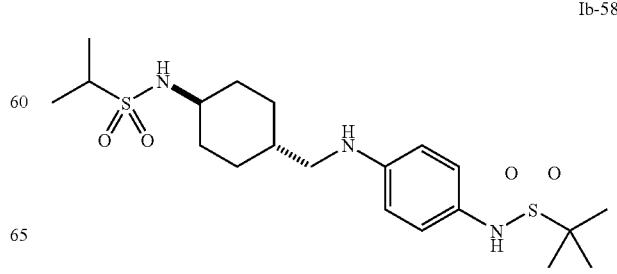
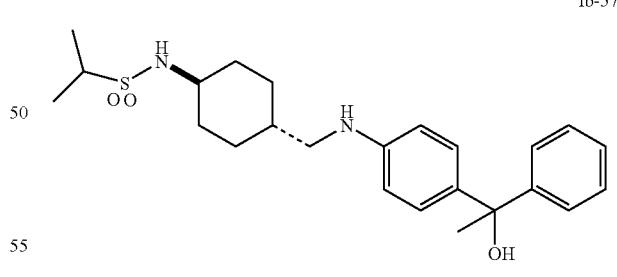
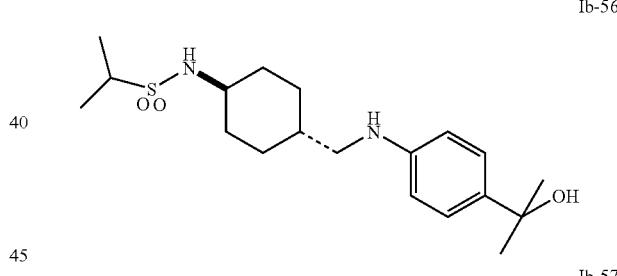
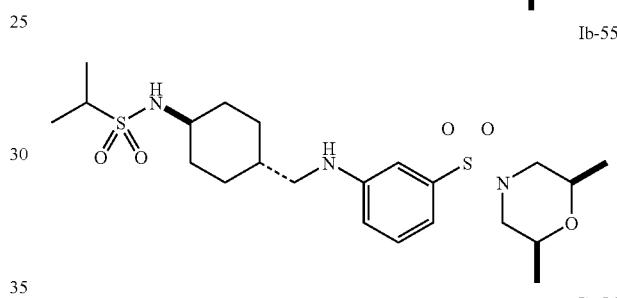
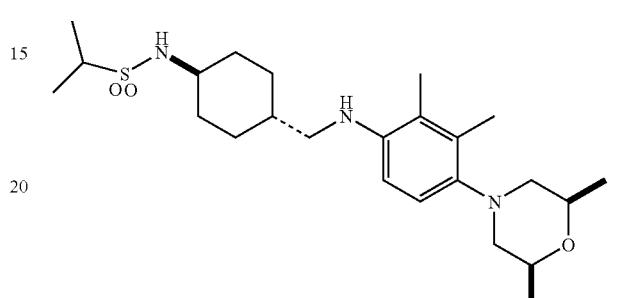
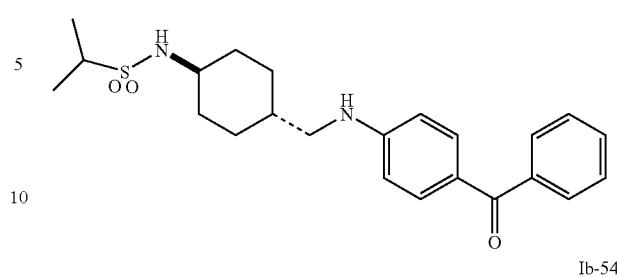
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Ib-48

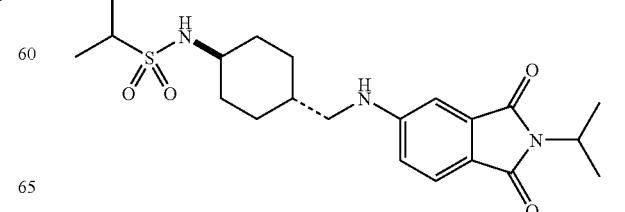
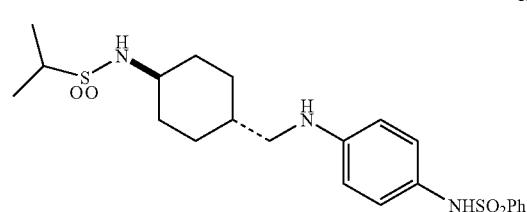
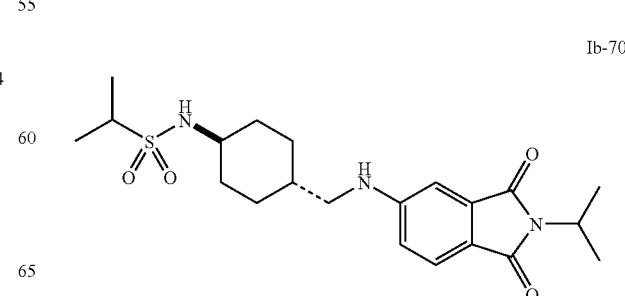
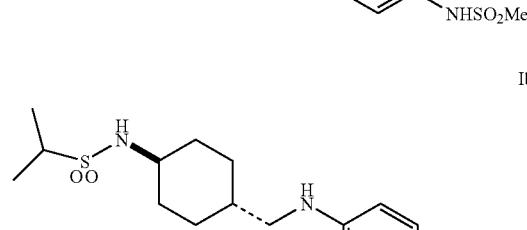
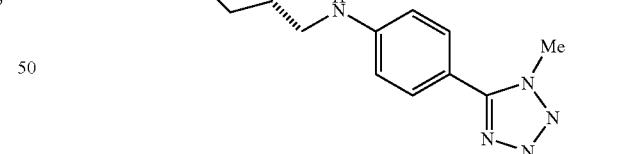
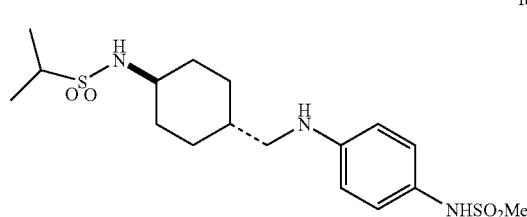
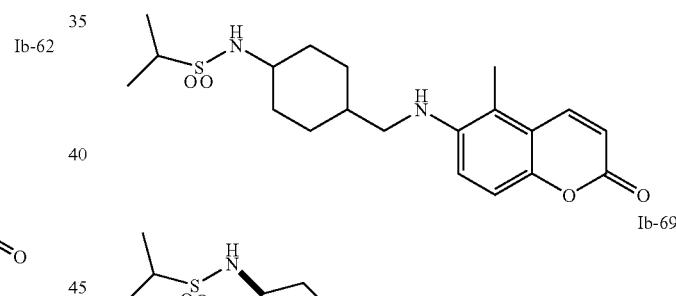
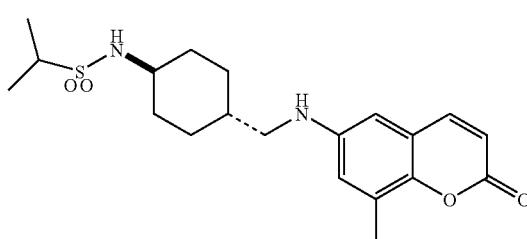
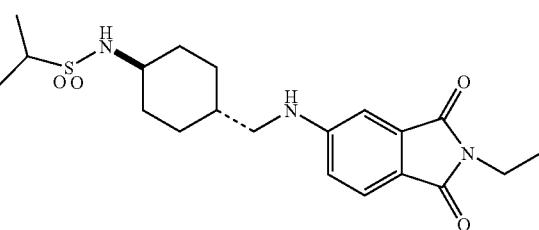
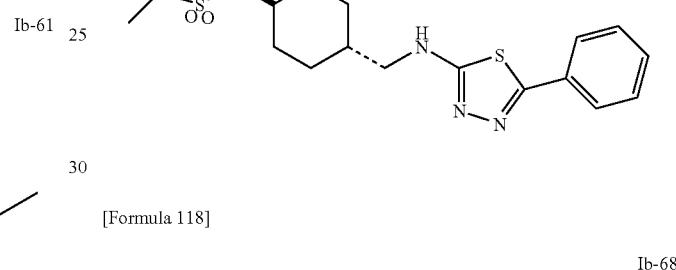
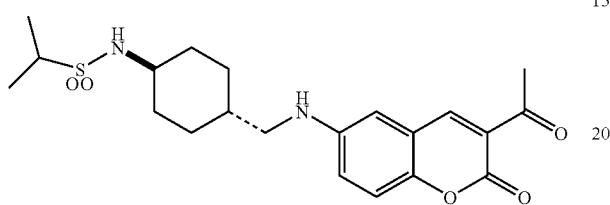
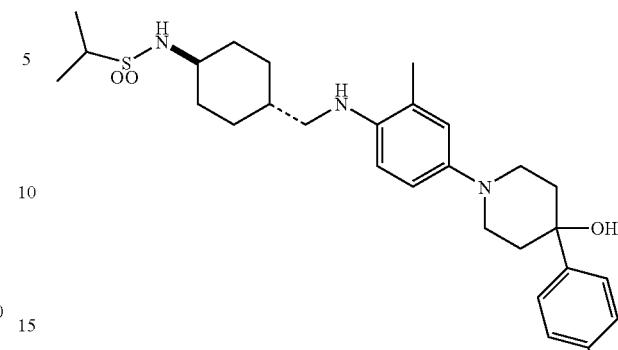
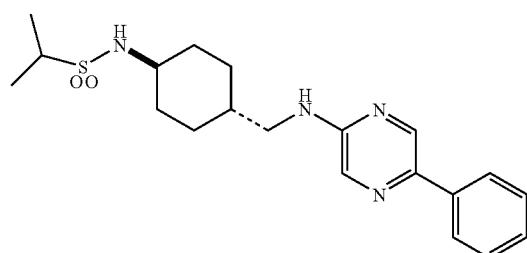
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197

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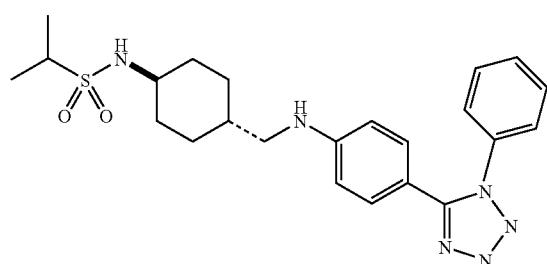
**198**

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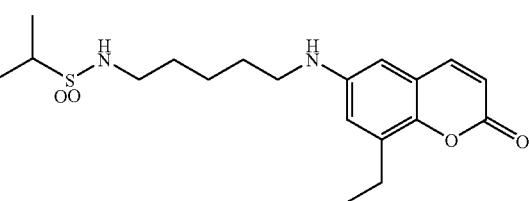
Ib-65

199

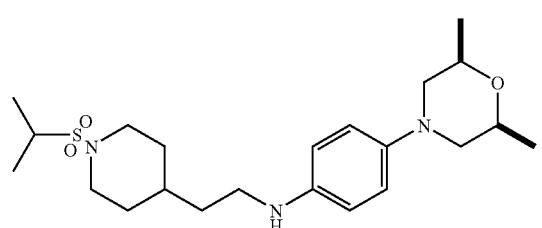
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**200**

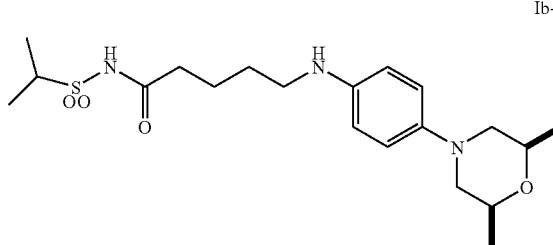
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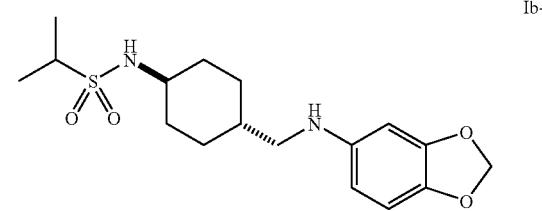
Ib-72 15



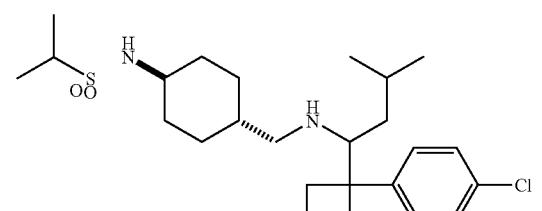
Ib-73



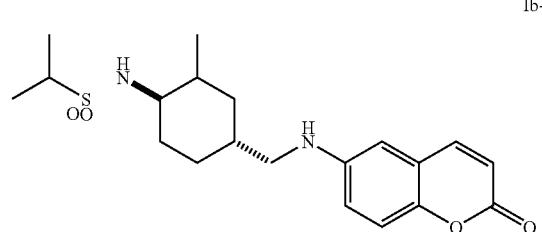
Ib-74



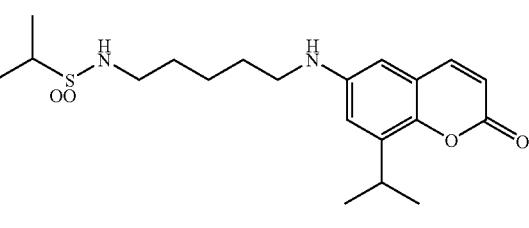
Ib-75



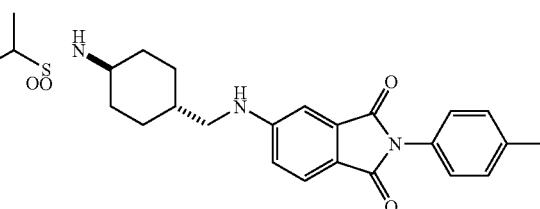
Ib-76



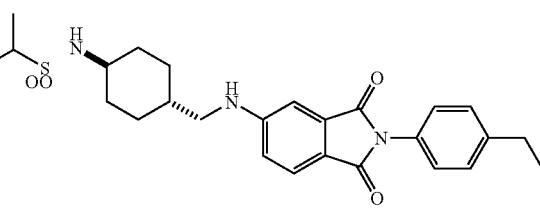
Ib-77



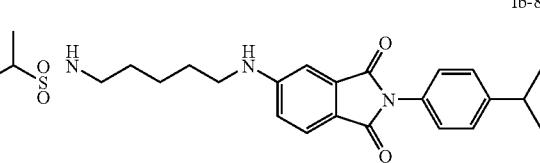
Ib-78



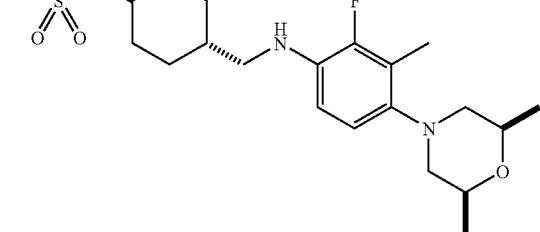
Ib-79



Ib-80



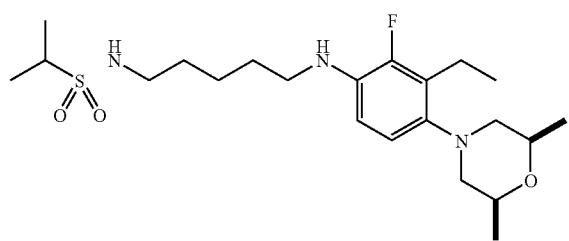
Ib-81



Ib-82

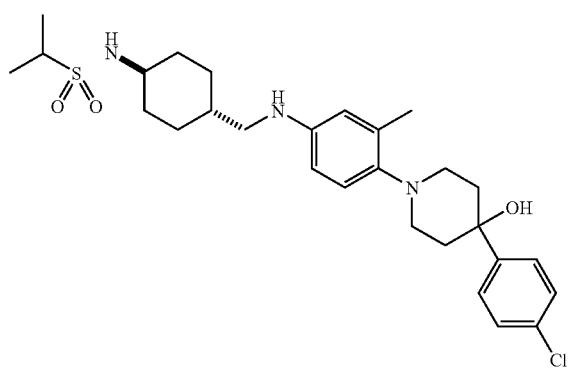
201

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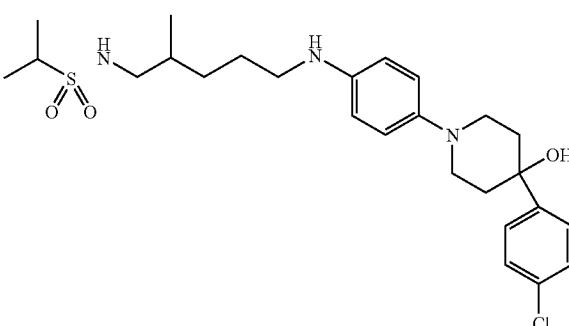


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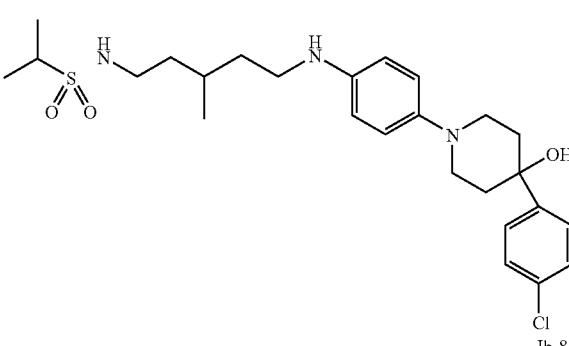
[Formula 119]



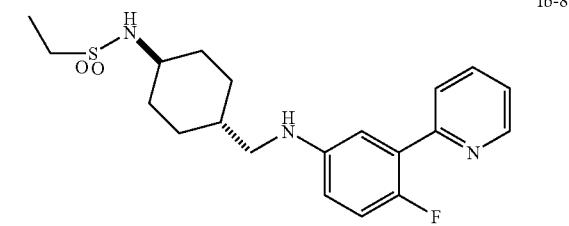
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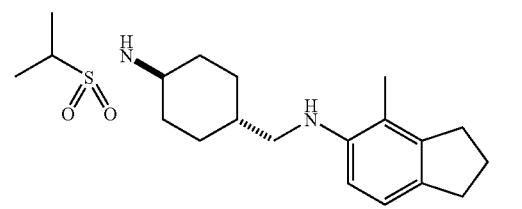
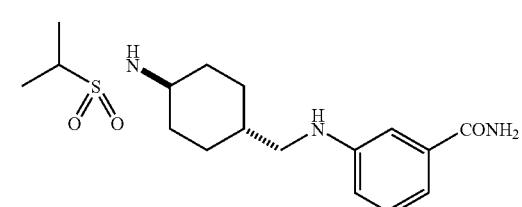
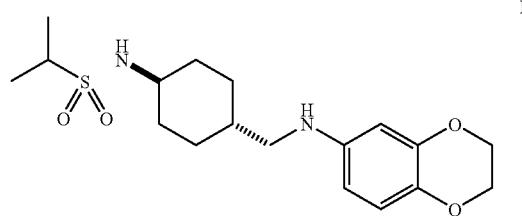
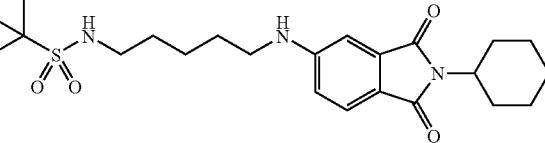
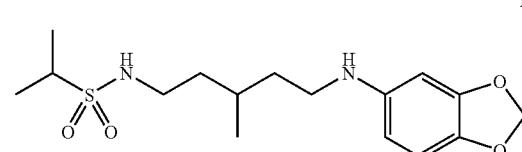
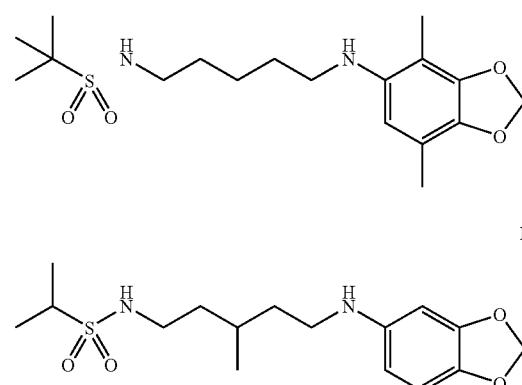
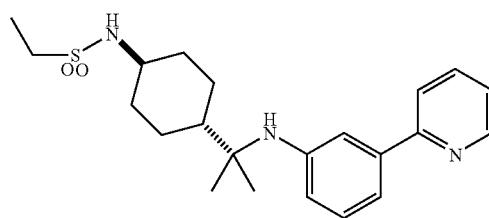
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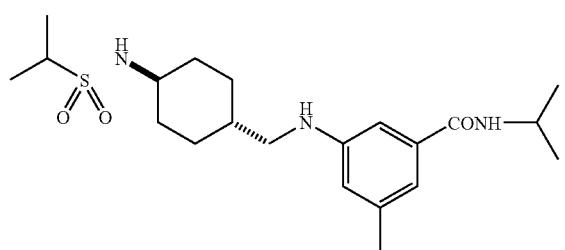
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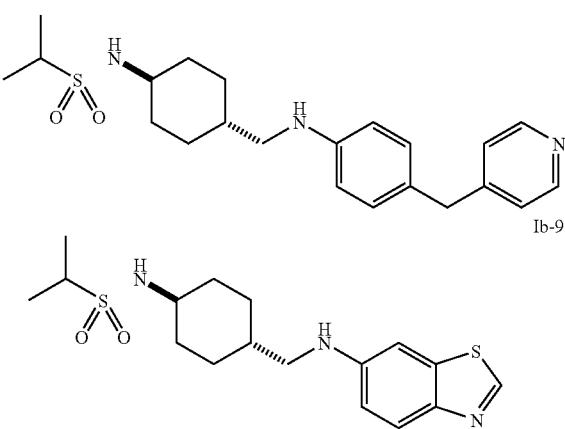


203

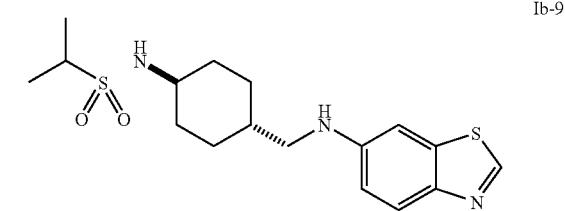
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Ib-95

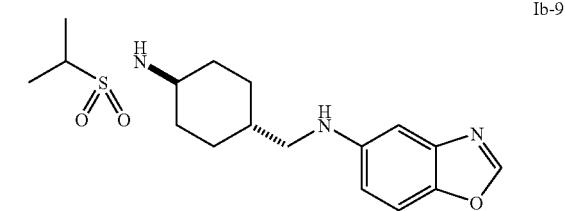
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Ib-96

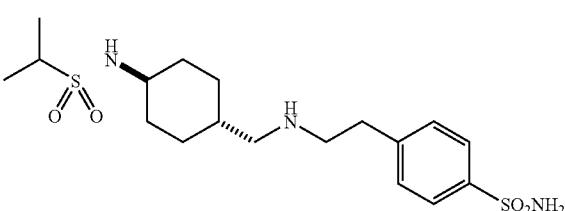
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Ib-97

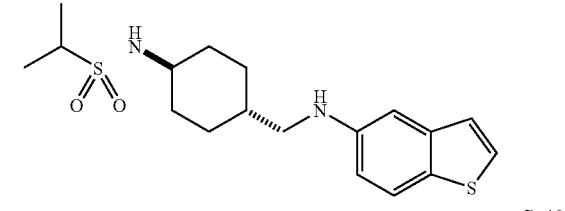
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Ib-98

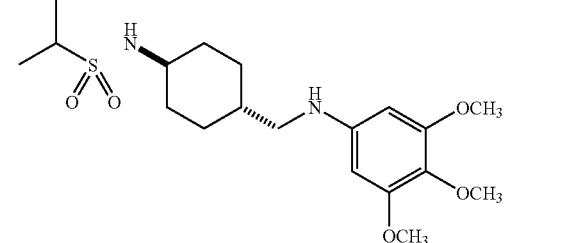
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Ib-99

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Ib-100

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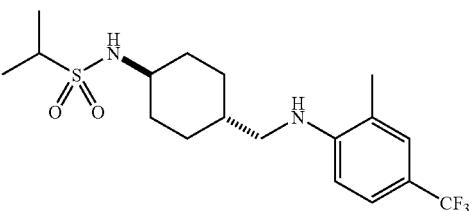


Ib-101

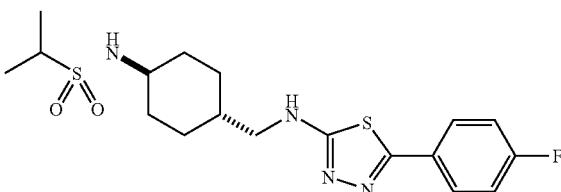
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65**204**

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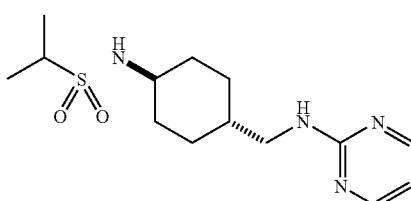
Ib-102



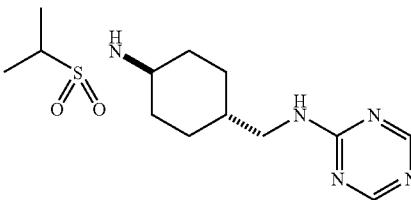
Ib-103



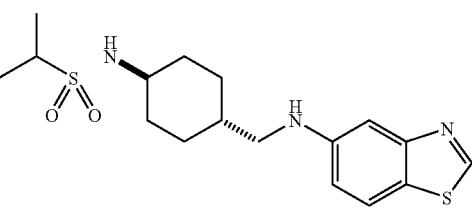
Ib-104



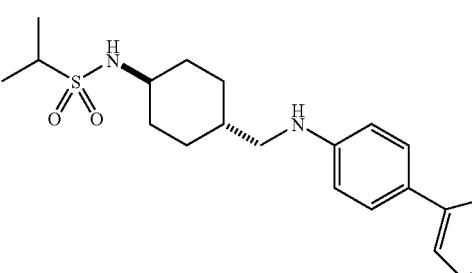
Ib-105



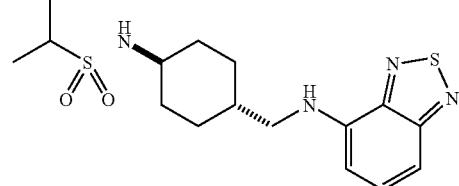
Ib-106



Ib-107



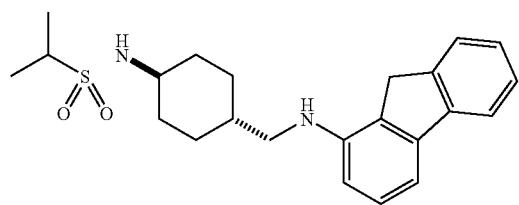
Ib-108



205

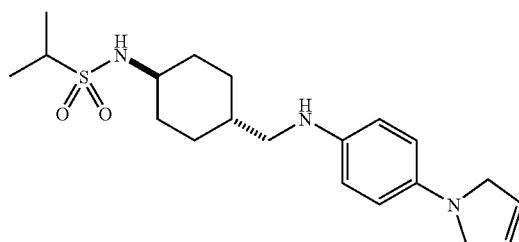
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Ib-109



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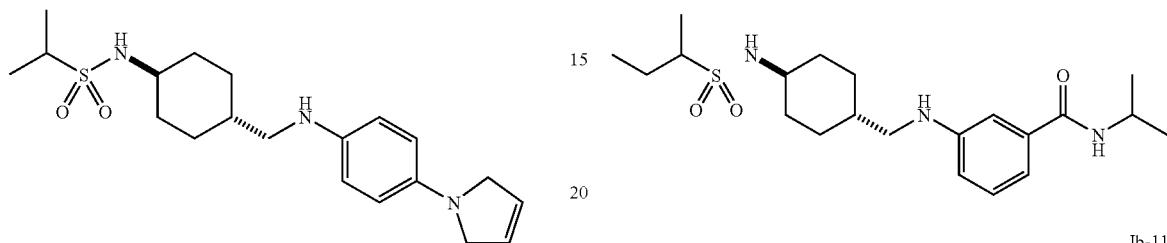
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Ib-110

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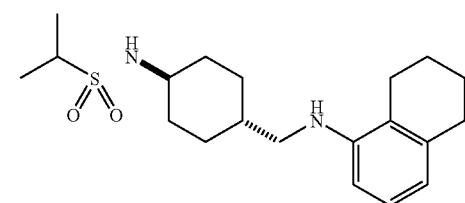
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Ib-116

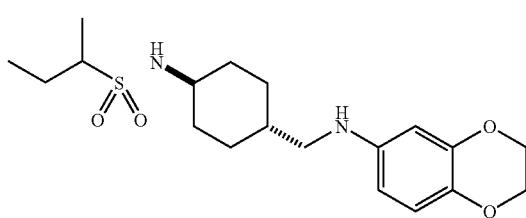
Ib-117

[Formula 120]

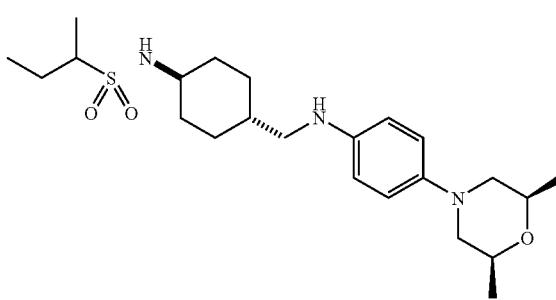


Ib-111 25

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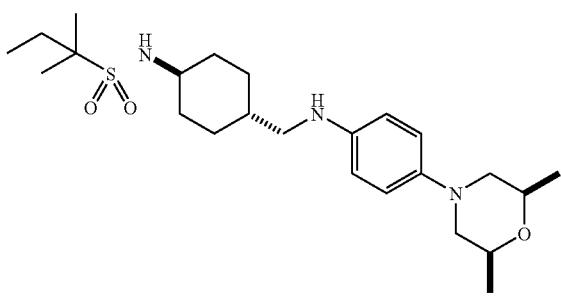
Ib-118



Ib-112 35

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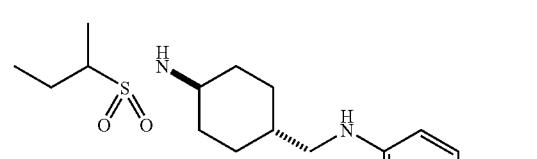
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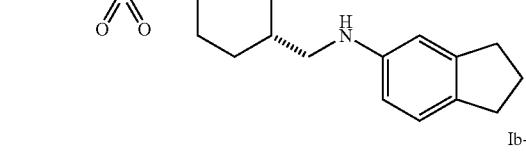
Ib-119

Ib-113

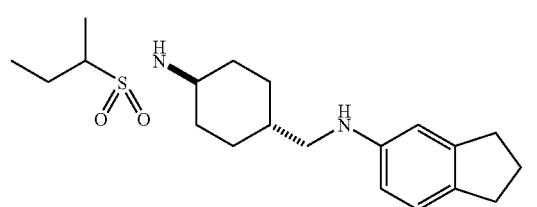
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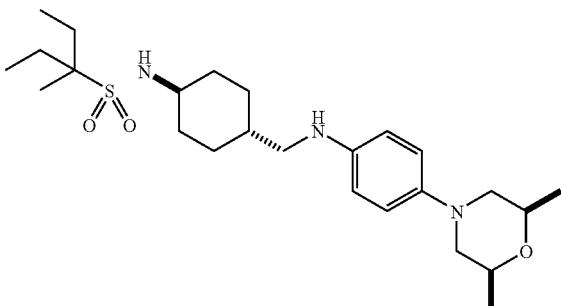


Ib-120



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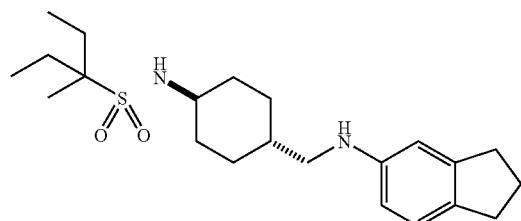
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Ib-115

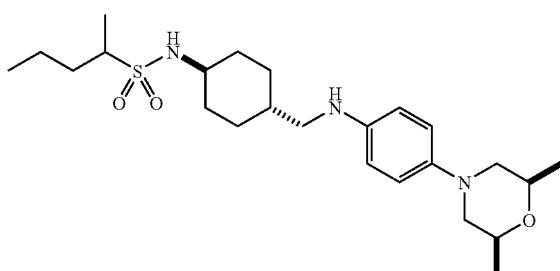
207
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Ib-121



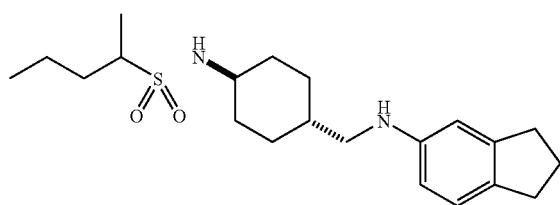
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Ib-122



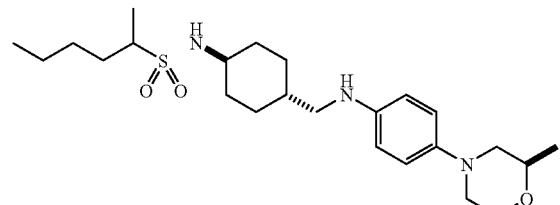
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Ib-123



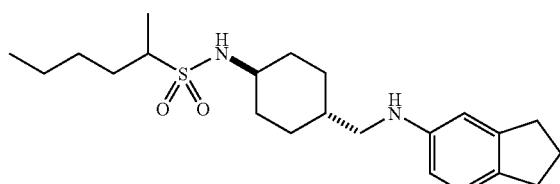
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Ib-124



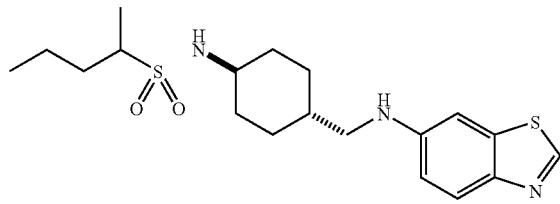
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Ib-125



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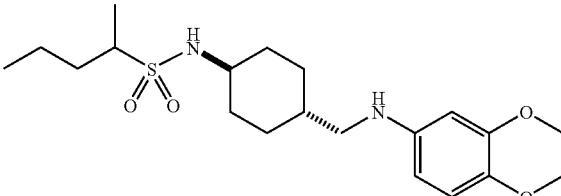
Ib-126



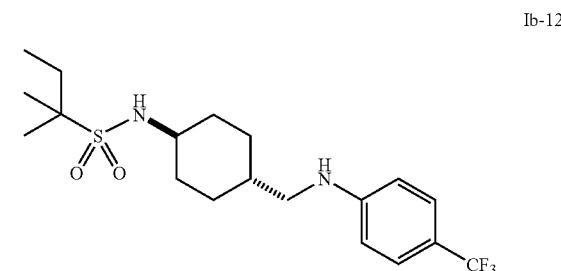
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208
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Ib-127

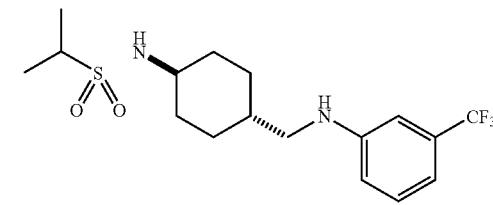


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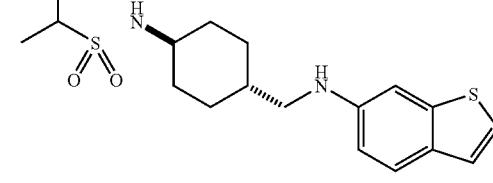
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Ib-129



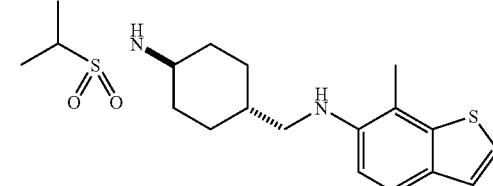
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Ib-130



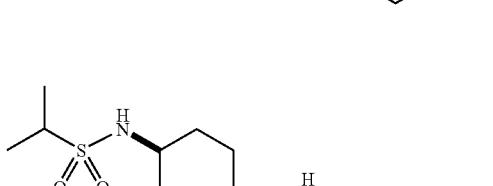
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Ib-131



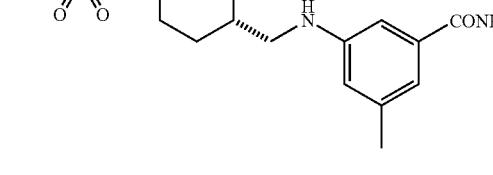
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Ib-132



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Ib-133

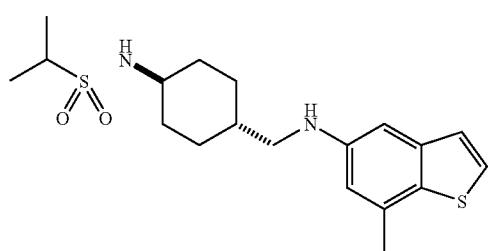


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209

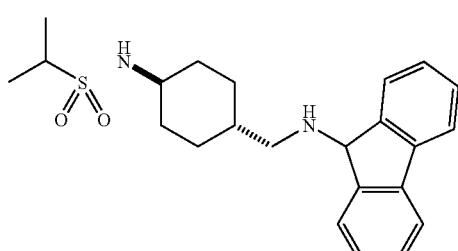
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[Formula 121]



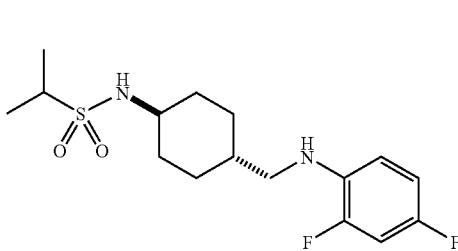
Ib-133

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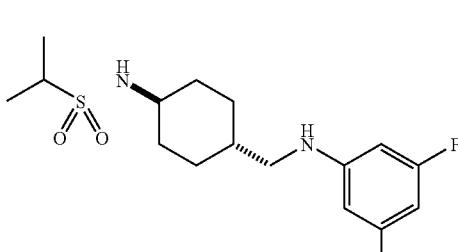
Ib-134

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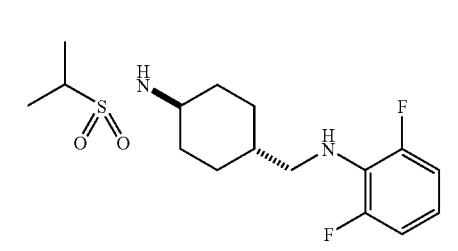
Ib-135

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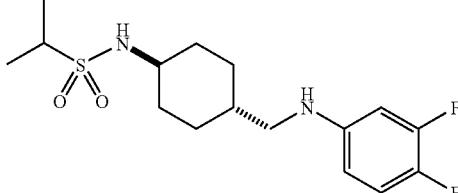
Ib-136

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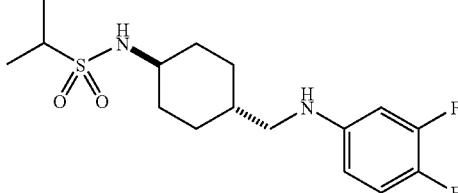
Ib-137

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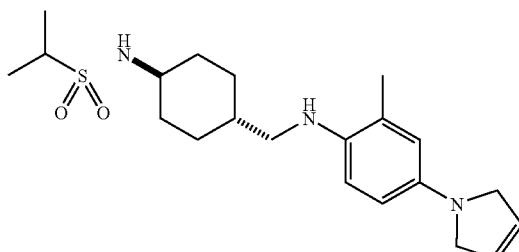
Ib-138

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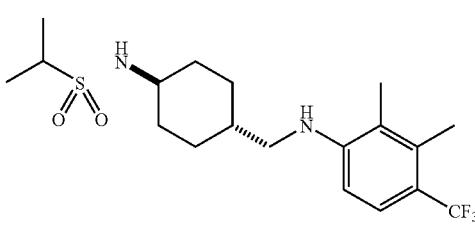
**210**

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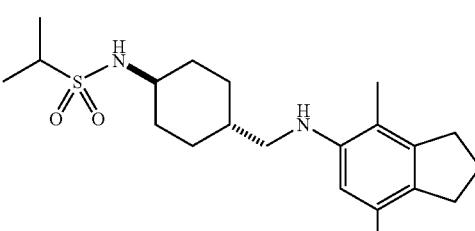
Ib-139



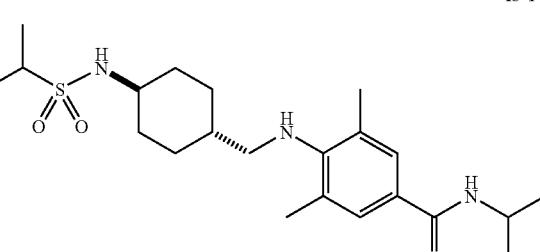
Ib-140



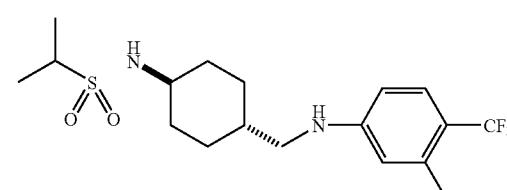
Ib-141



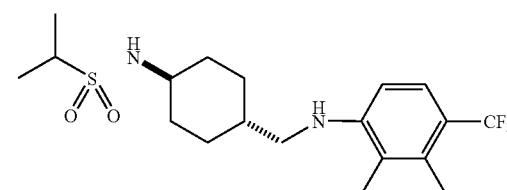
Ib-142



Ib-143

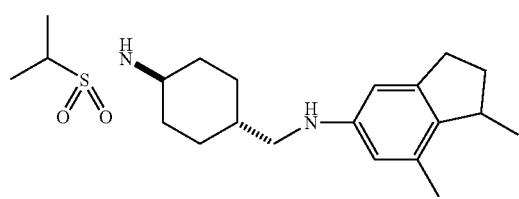


Ib-144



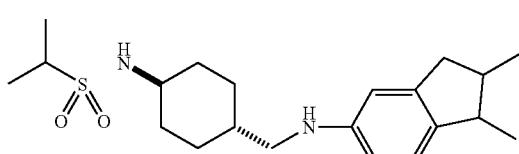
211

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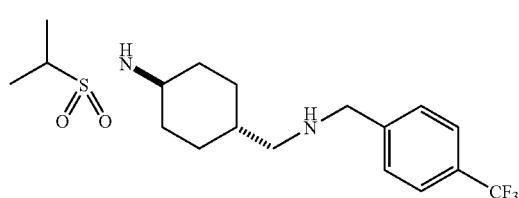
Ib-145

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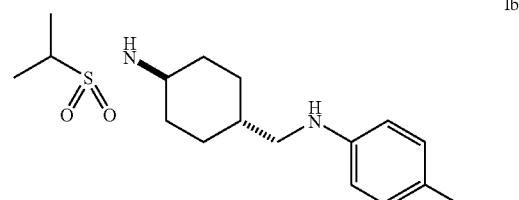
Ib-146

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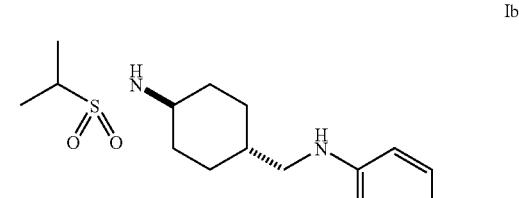
Ib-147

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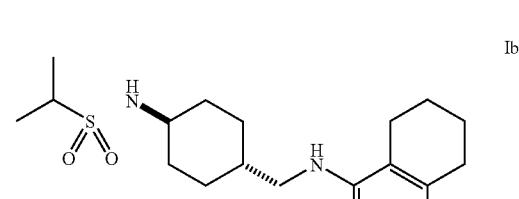
Ib-148

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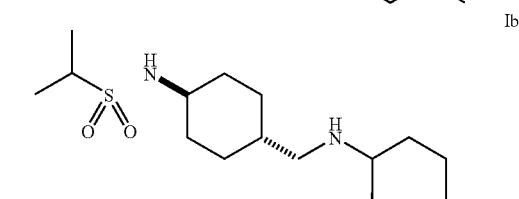
Ib-149

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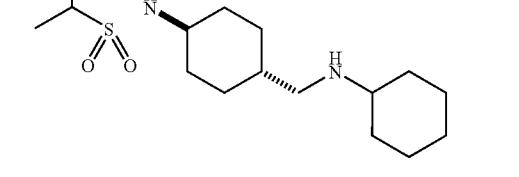
Ib-150

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Ib-151

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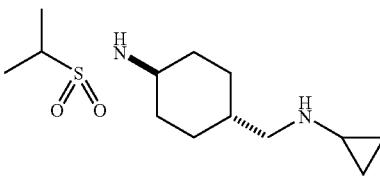


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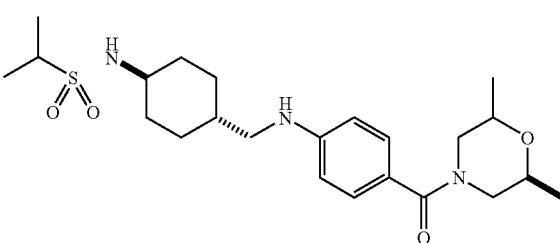
212

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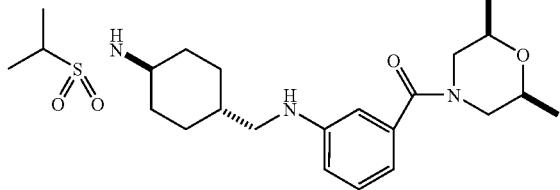


Ib-152

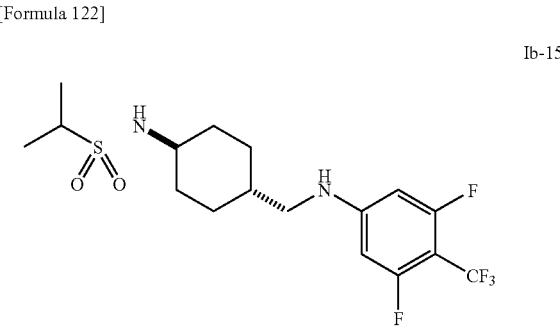
Ib-153



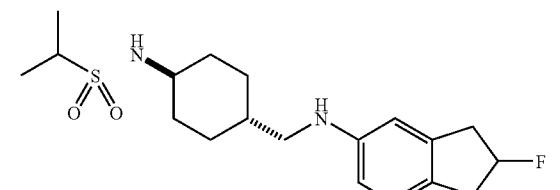
Ib-154



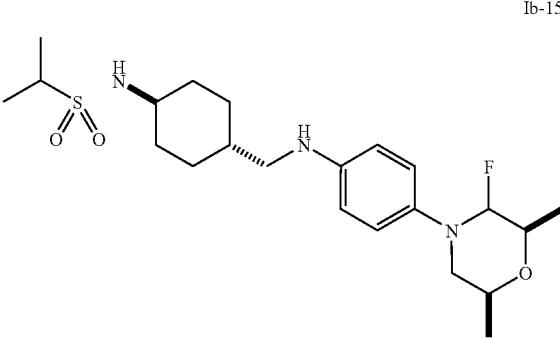
Ib-155



Ib-156



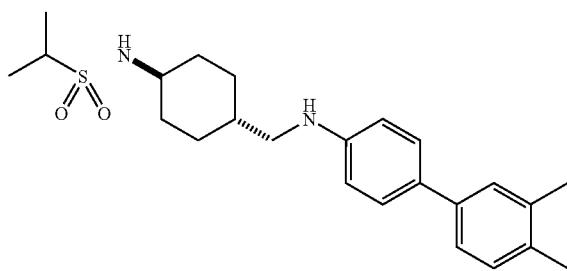
Ib-157



213

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Ib-158



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Ib-159

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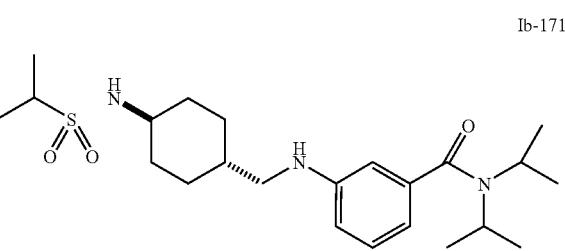
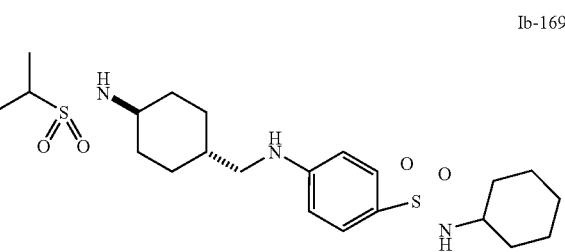
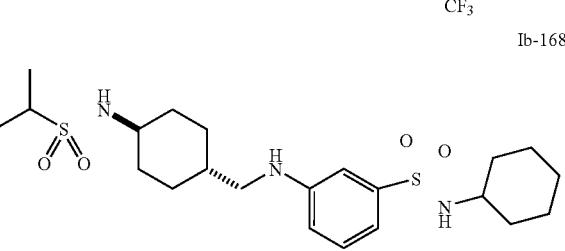
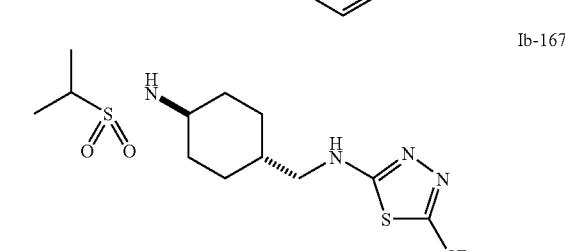
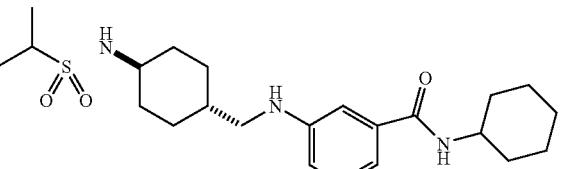
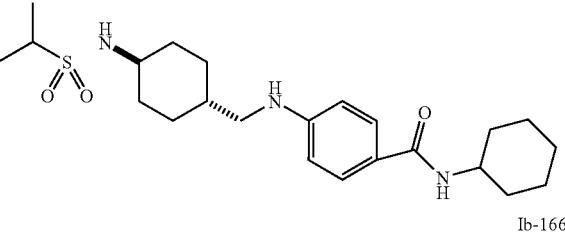
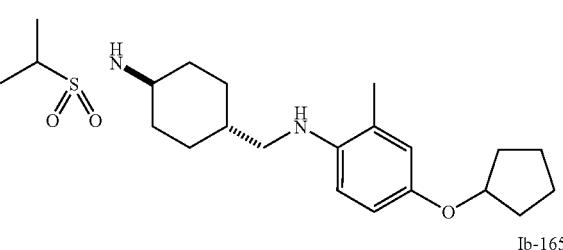
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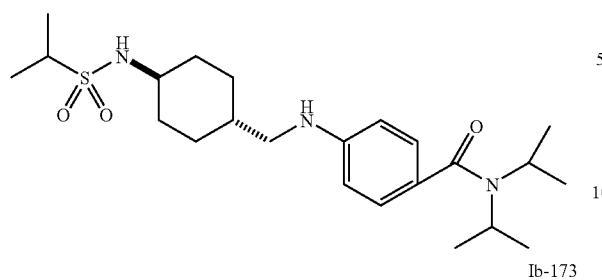
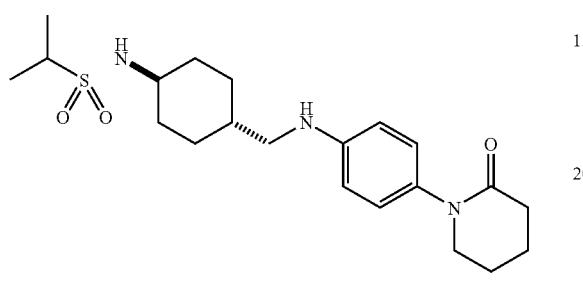
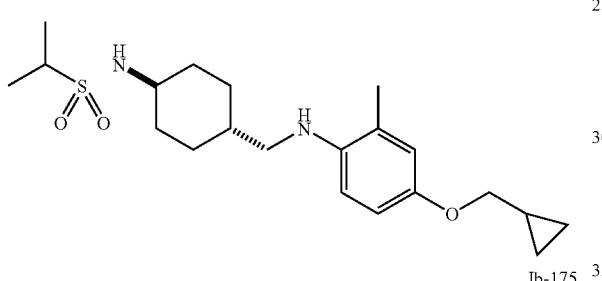
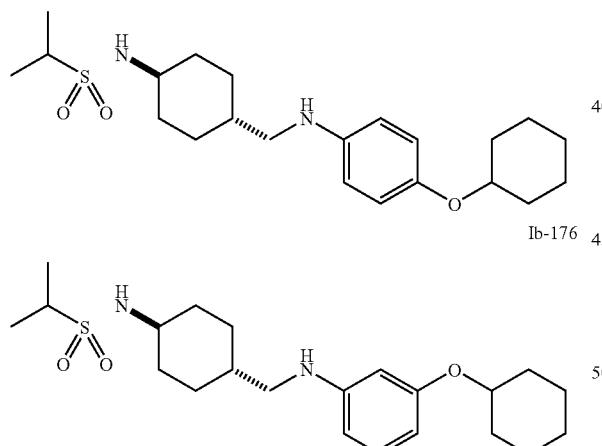
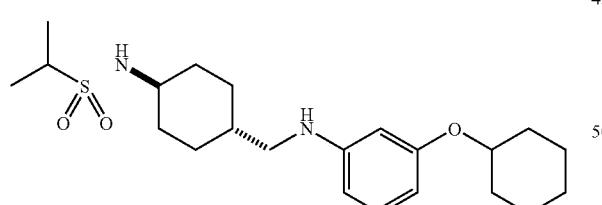
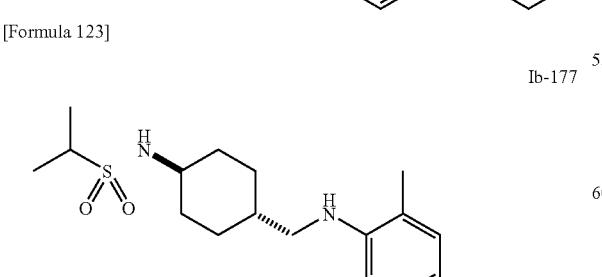
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Ib-164

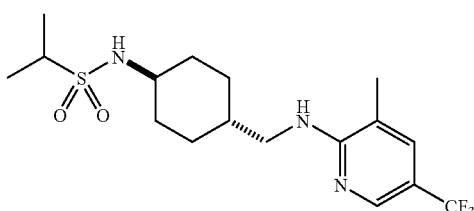
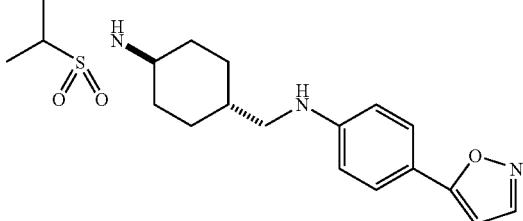
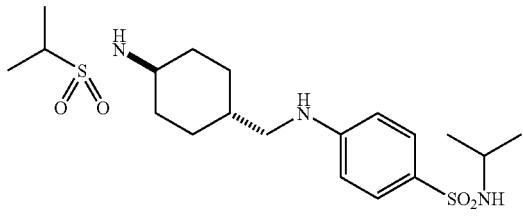
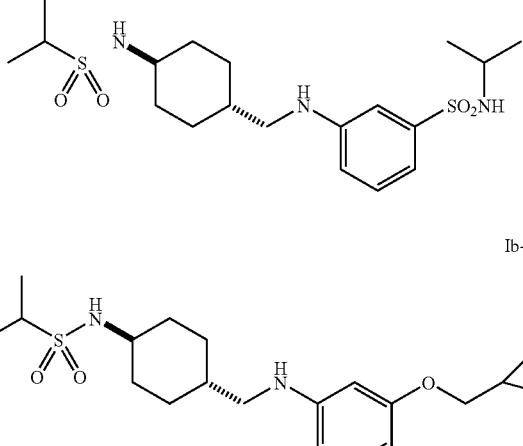


215

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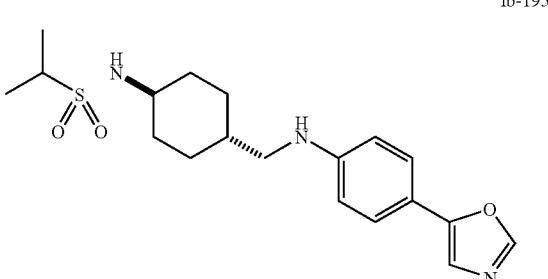
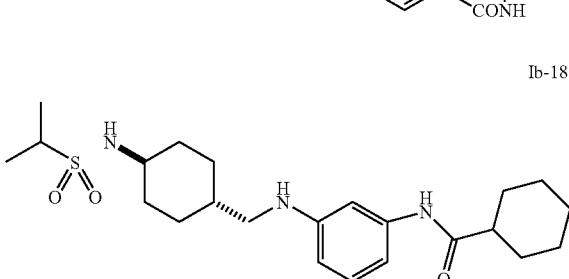
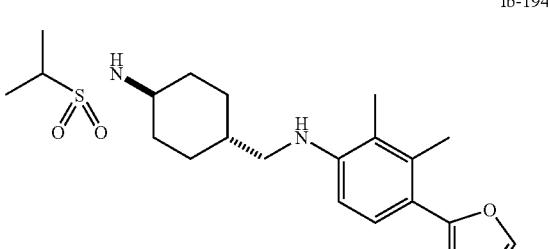
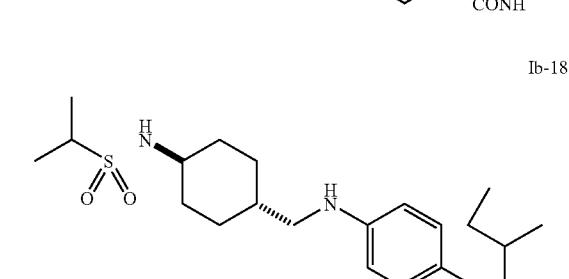
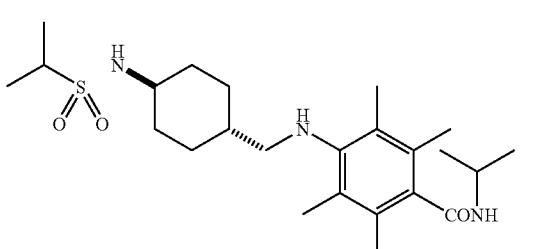
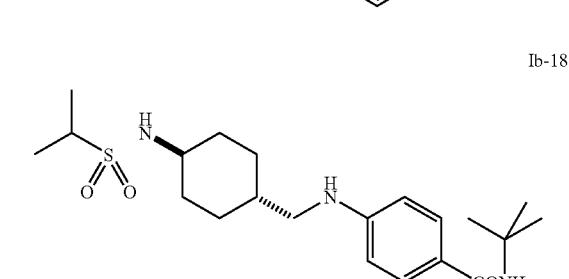
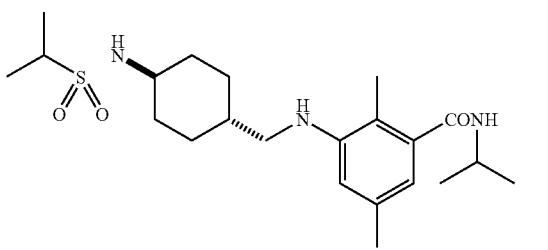
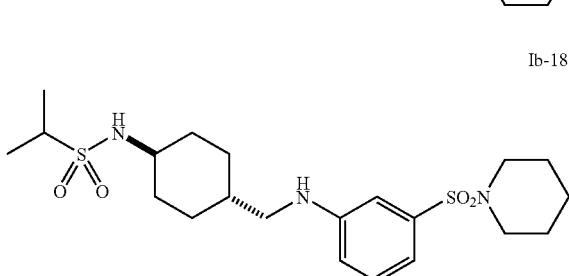
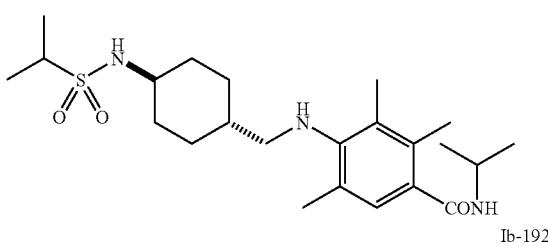
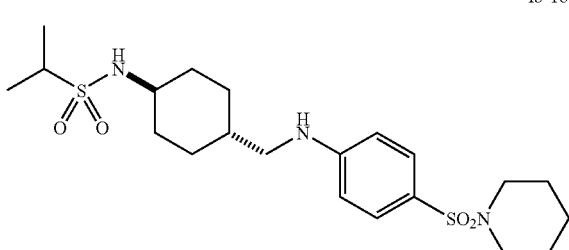
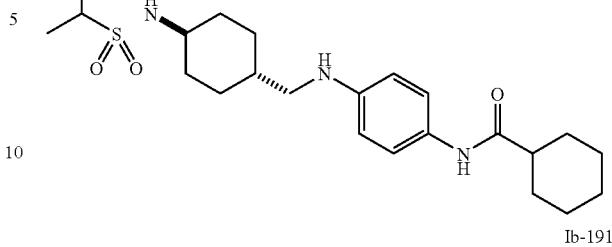
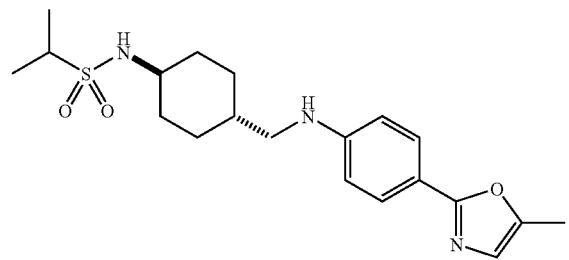
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[Formula 123]

217

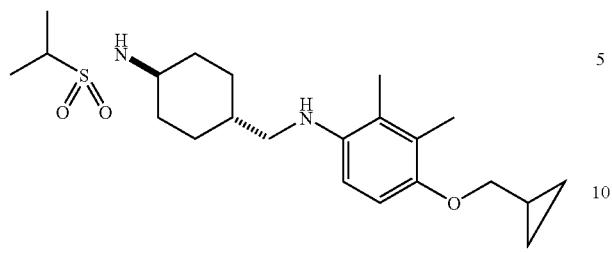
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219

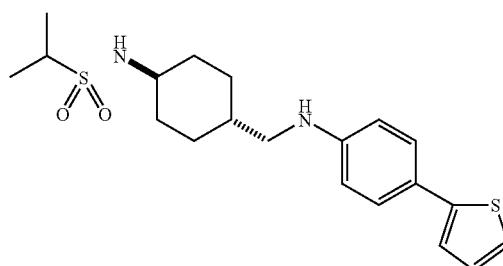
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Ib-196

**220**

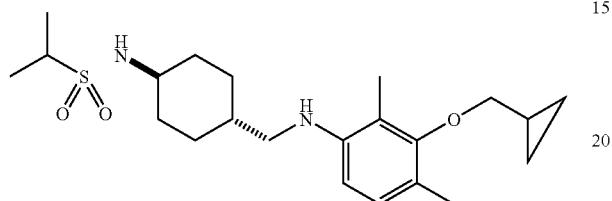
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Ib-202



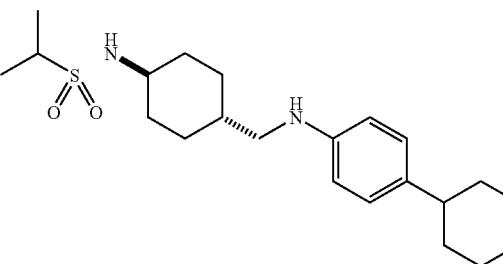
Ib-197

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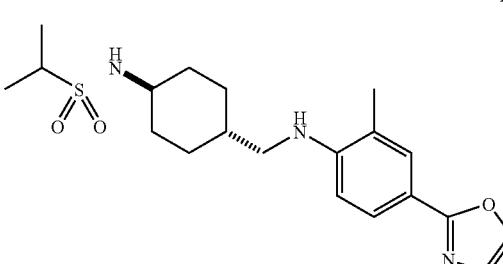
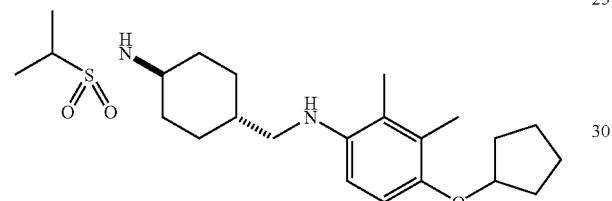


Ib-198

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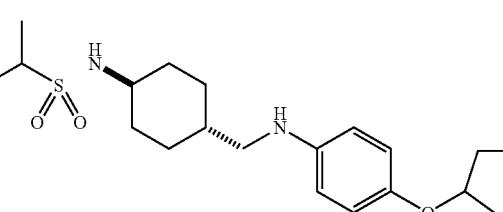
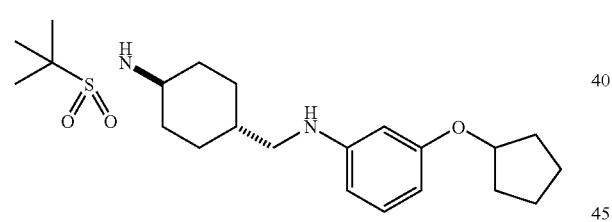
Ib-204



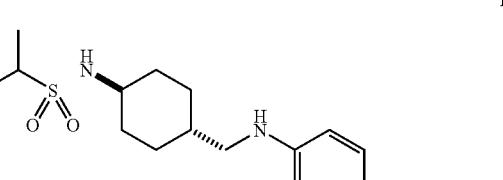
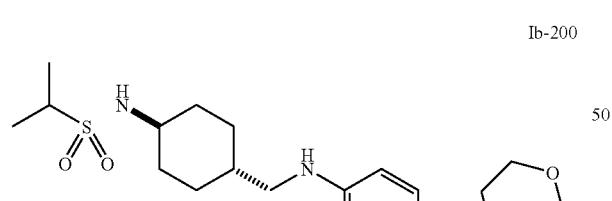
[Formula 124]

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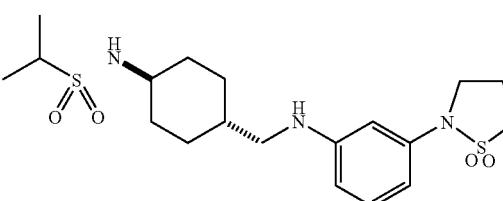
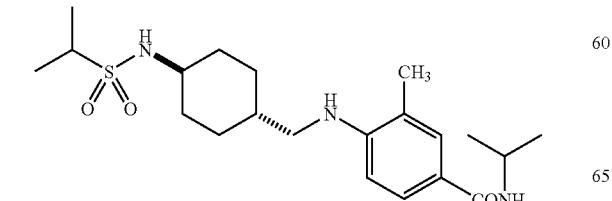
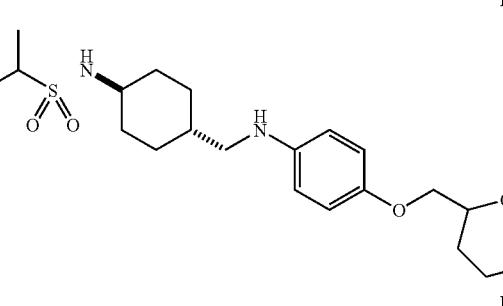
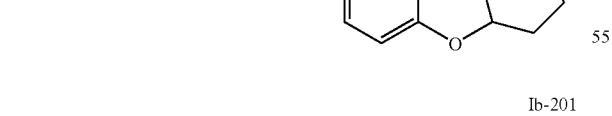
Ib-199



Ib-206



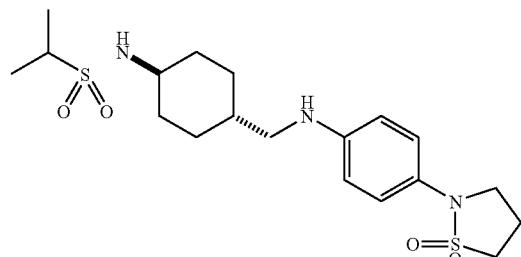
Ib-207



221

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Ib-208

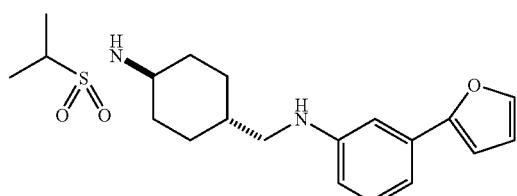


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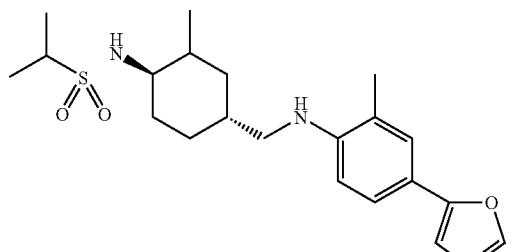
Ib-209



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Ib-210

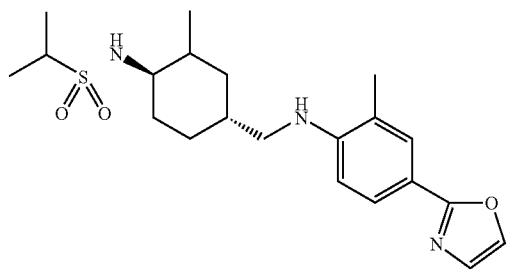


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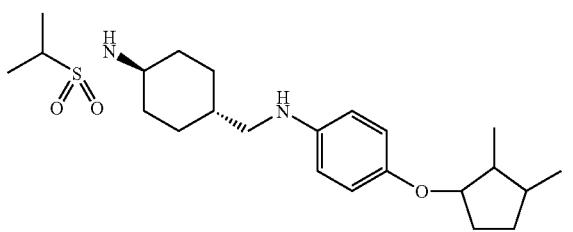
Ib-211



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Ib-212



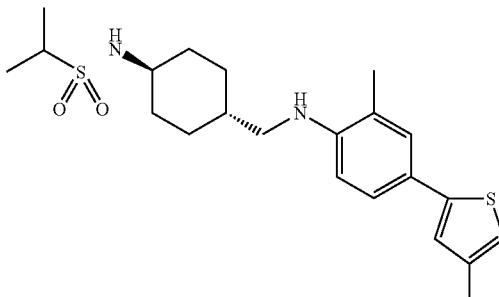
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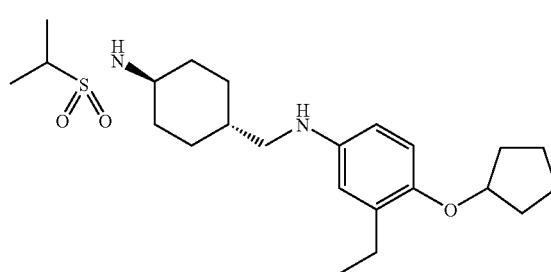
222

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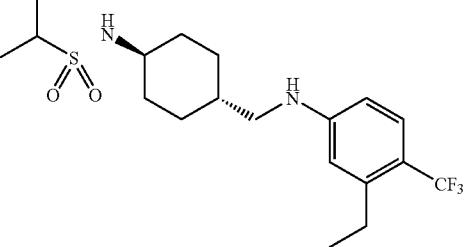
Ib-213



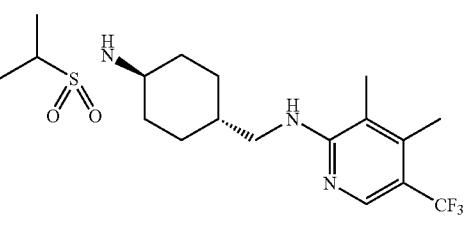
Ib-214



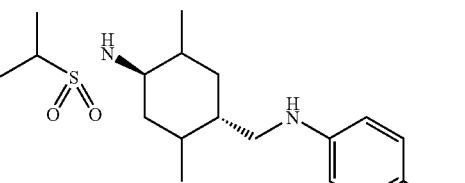
Ib-215



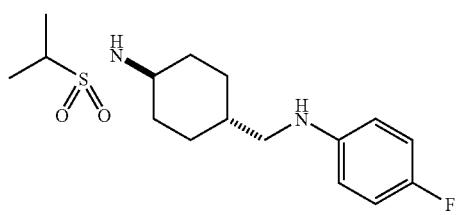
Ib-216



Ib-219

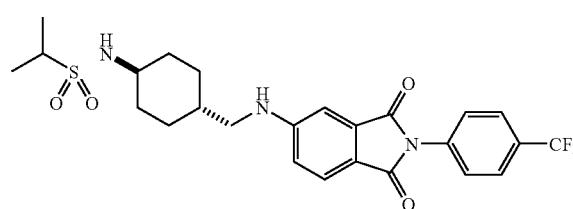
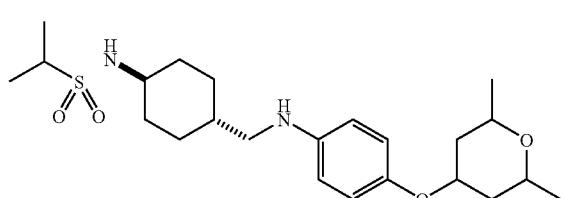
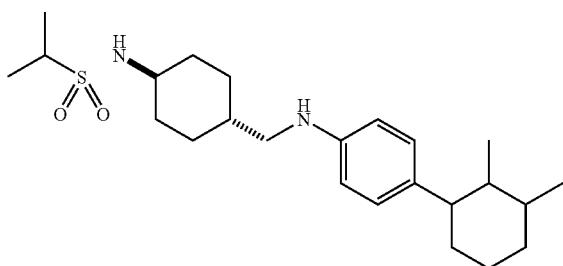
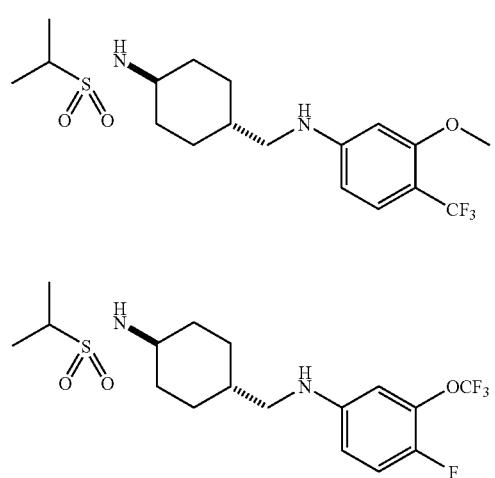
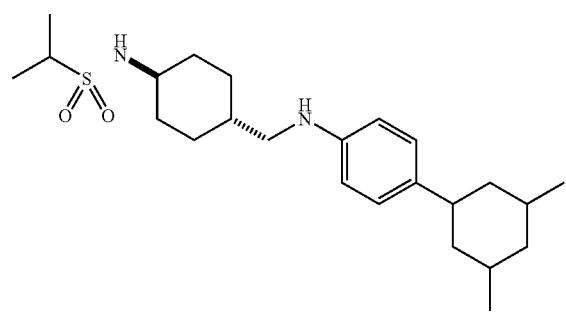


Ib-220



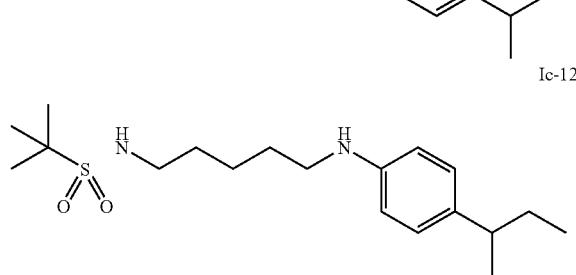
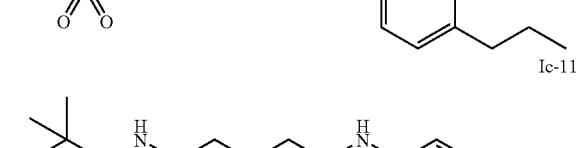
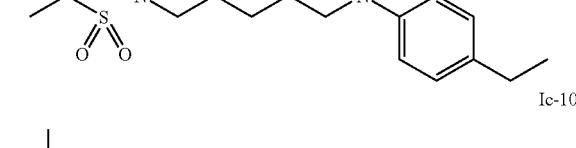
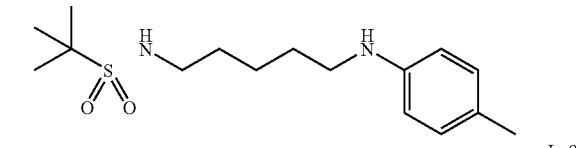
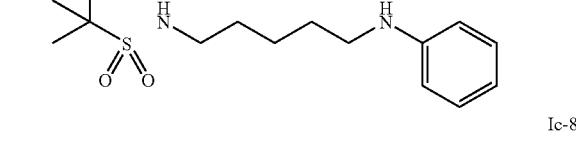
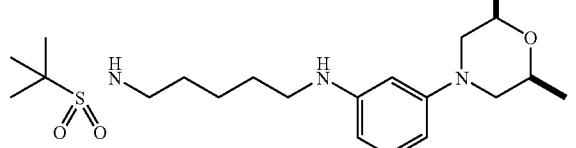
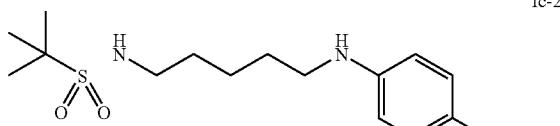
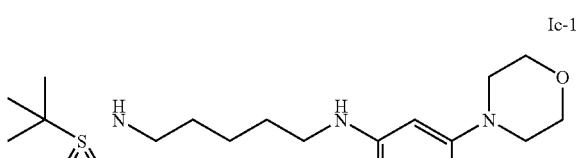
223

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**224**

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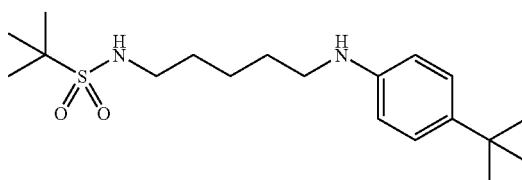
[Formula 125]



225

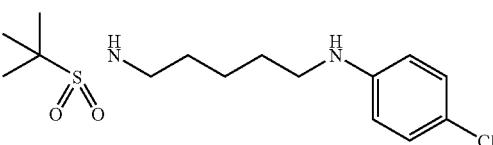
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Ic-13



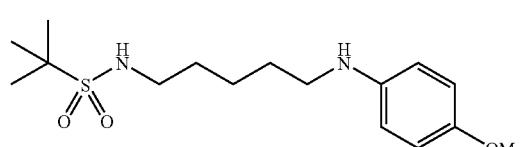
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Ic-14



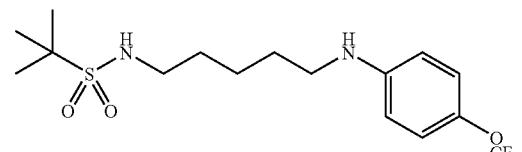
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[Formula 126]



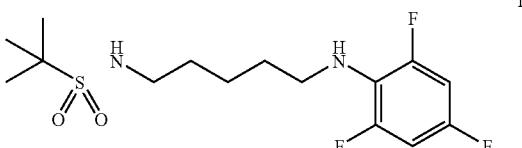
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Ic-25



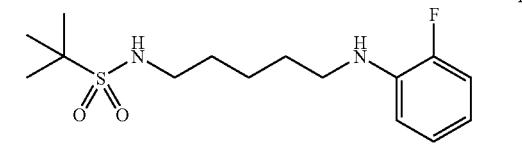
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Ic-18



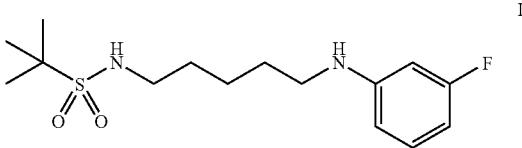
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Ic-19



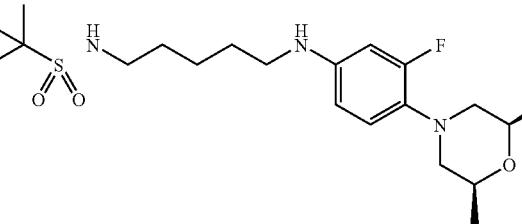
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Ic-20



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Ic-21



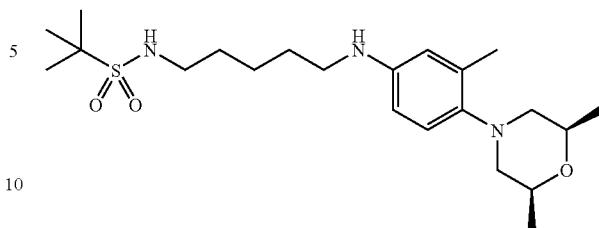
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226

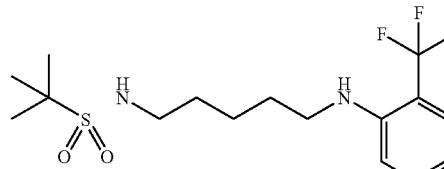
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Ic-22



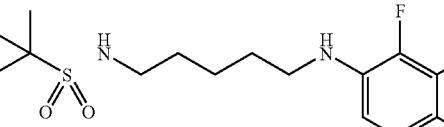
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Ic-23



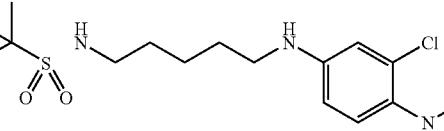
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Ic-24



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Ic-25



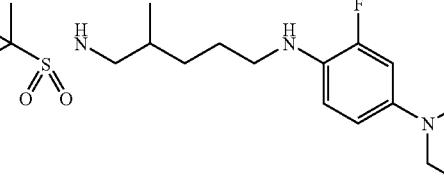
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Ic-26



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Ic-27



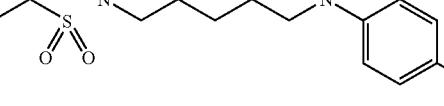
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Ic-28



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Ic-29

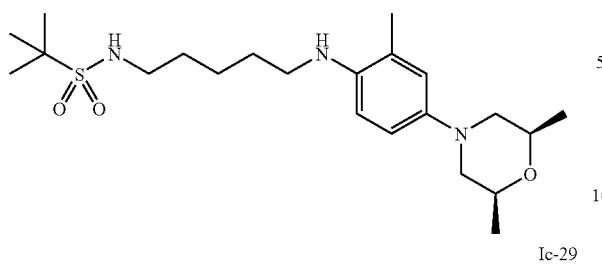


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227

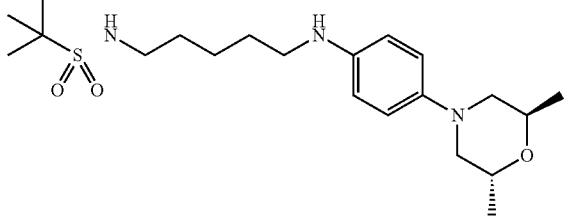
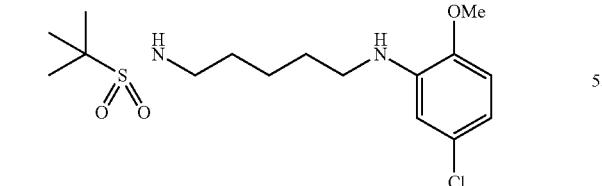
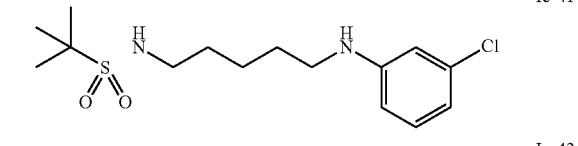
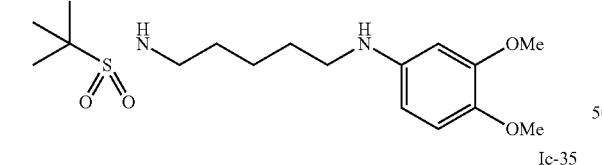
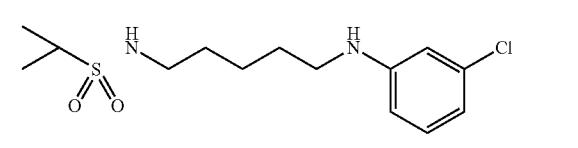
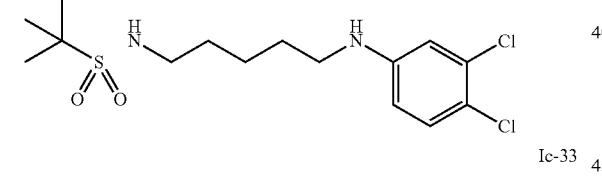
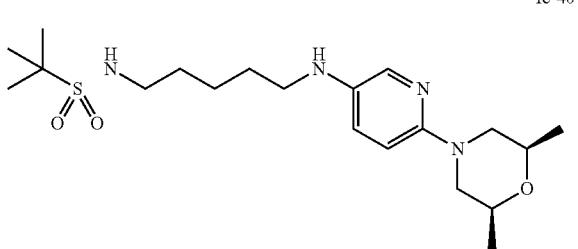
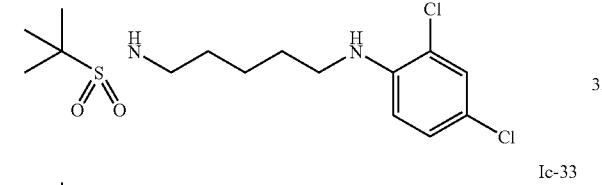
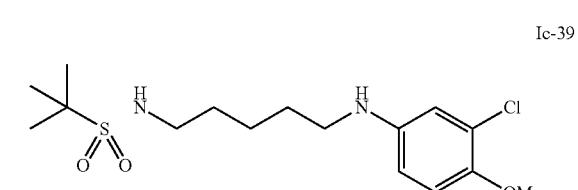
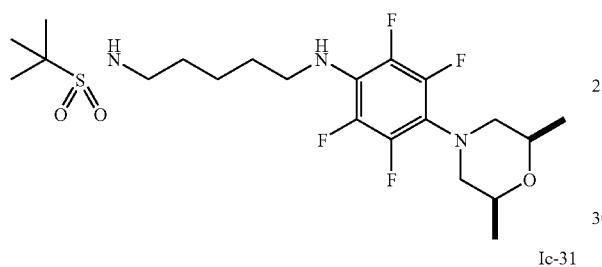
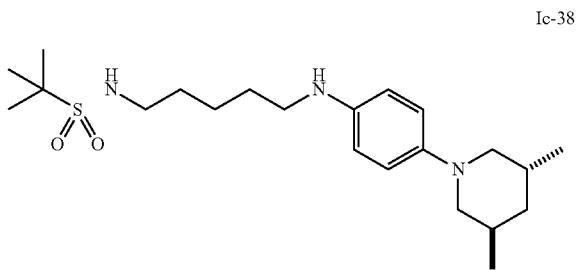
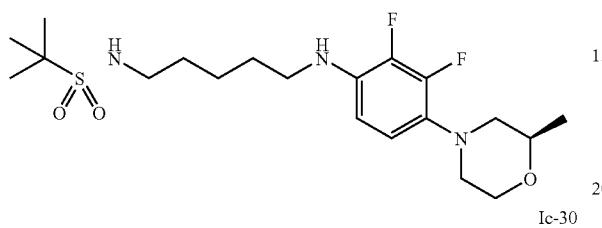
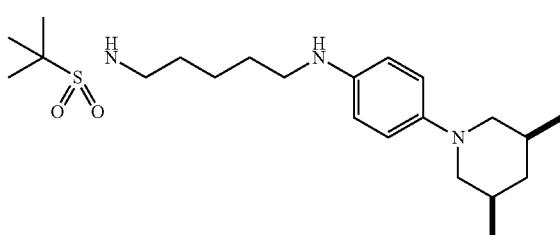
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Ic-28

**228**

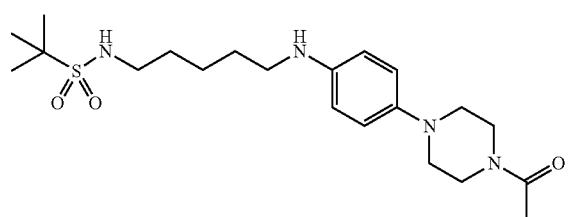
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Ic-37

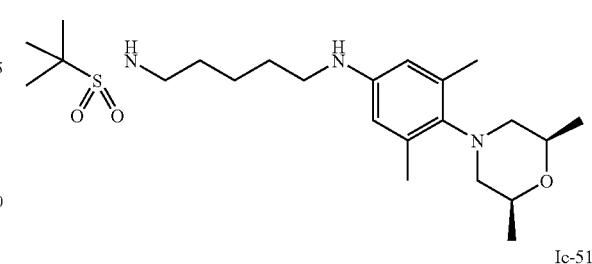
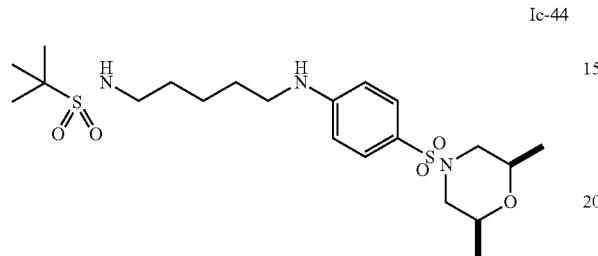
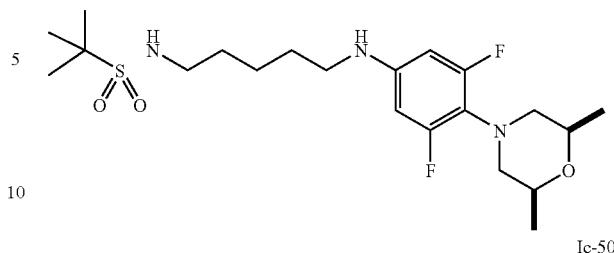


229

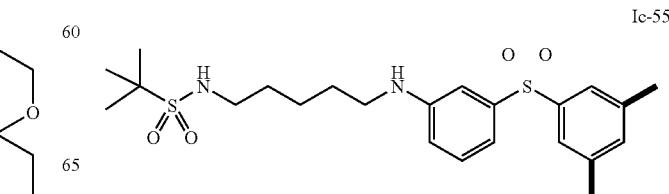
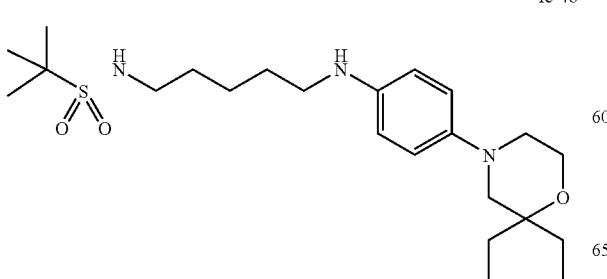
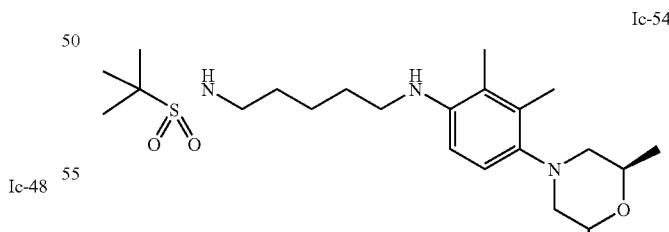
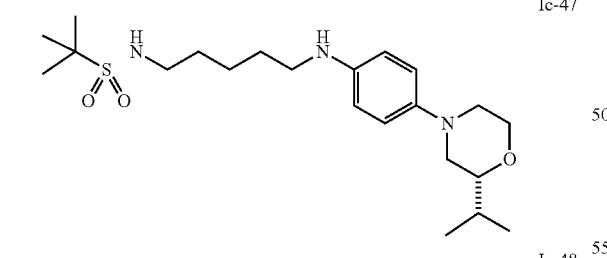
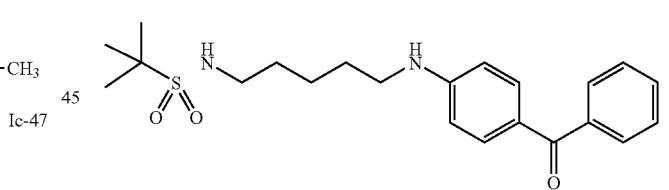
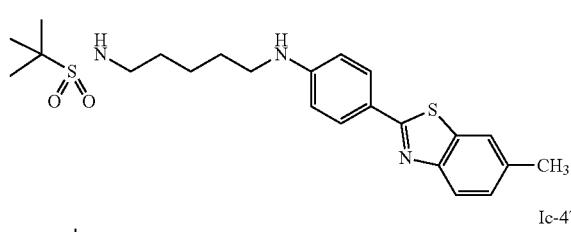
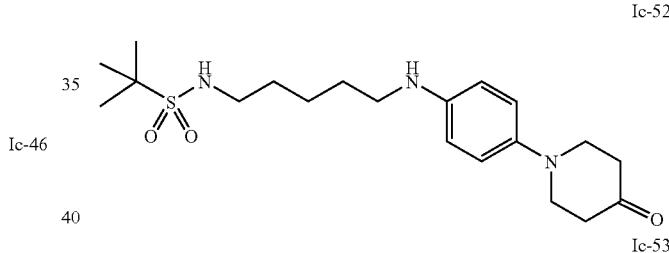
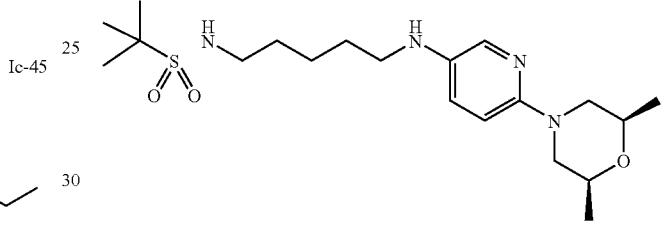
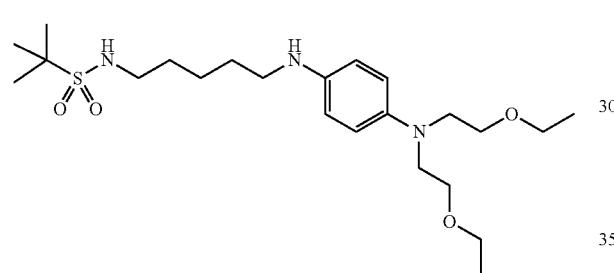
-continued

**230**

-continued

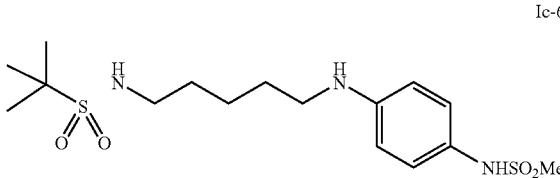
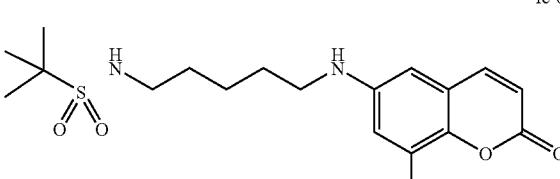
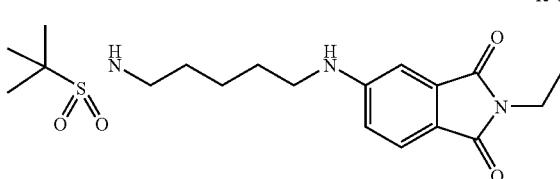
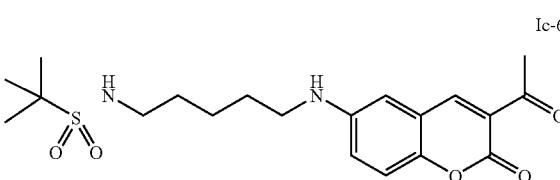
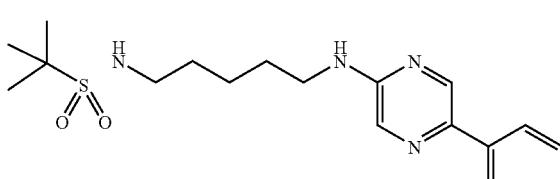
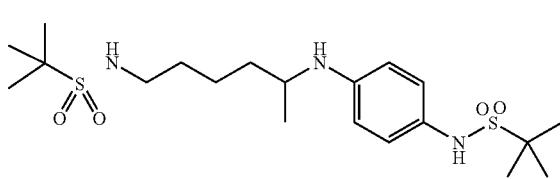
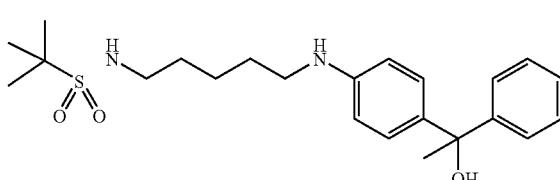
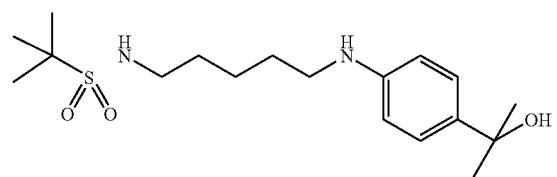


[Formula 127]



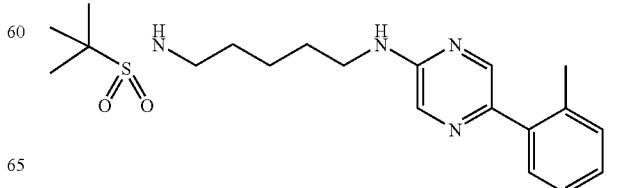
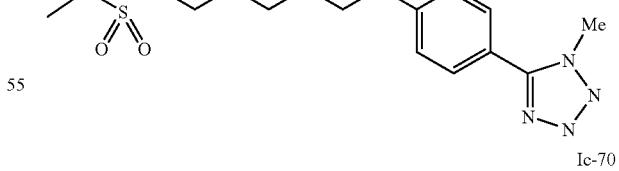
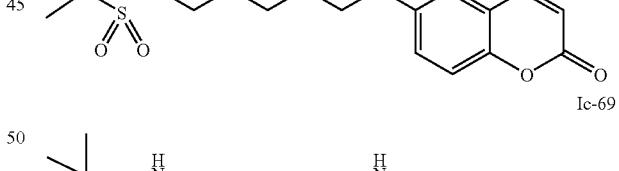
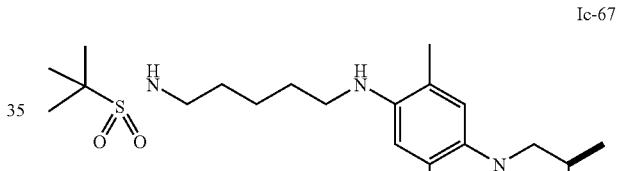
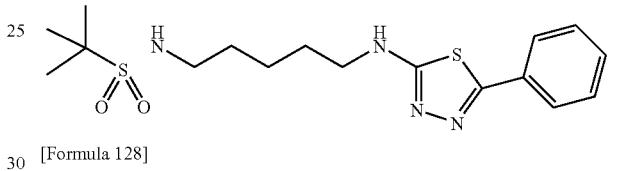
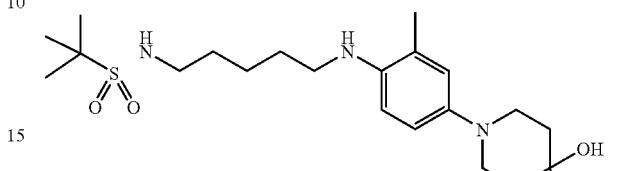
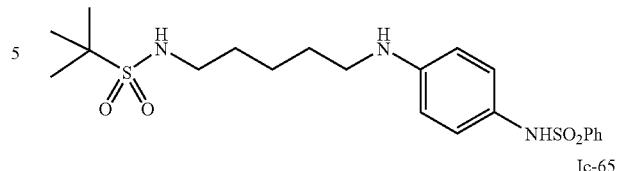
231

-continued

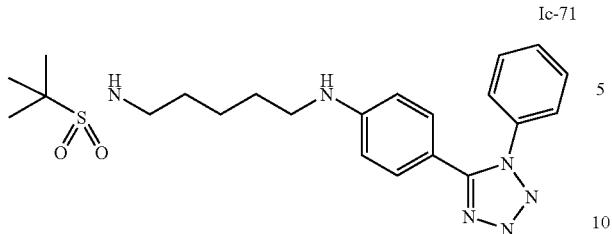
**232**

-continued

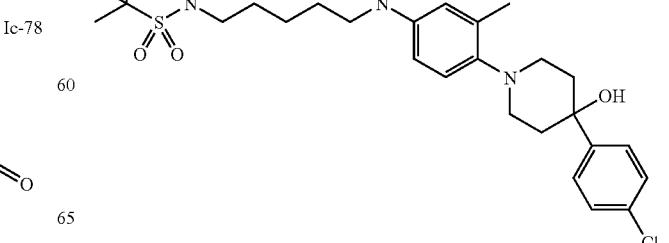
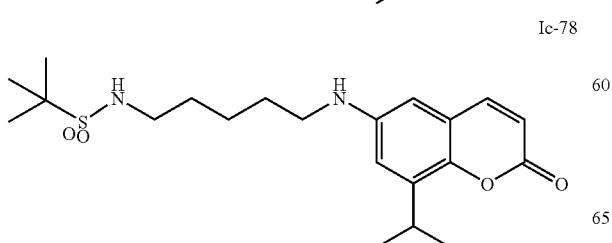
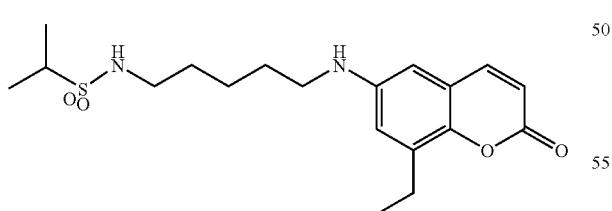
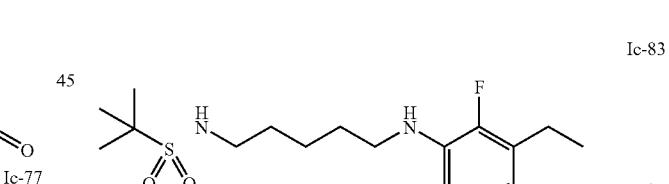
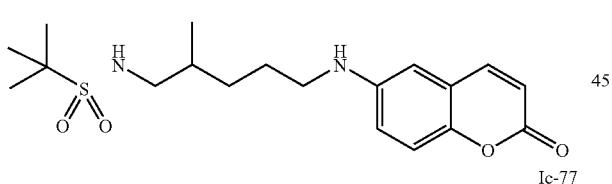
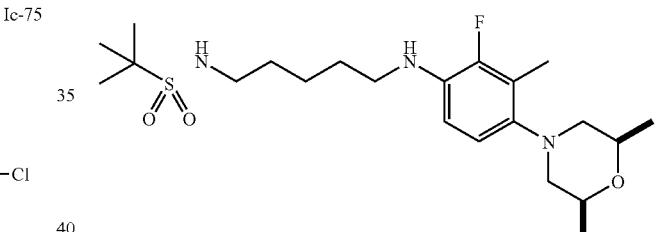
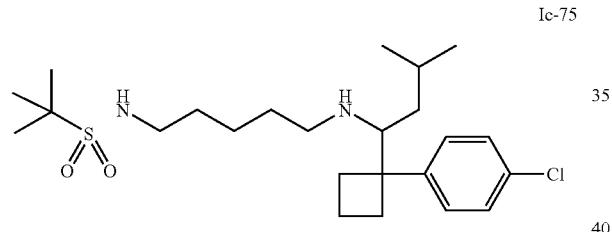
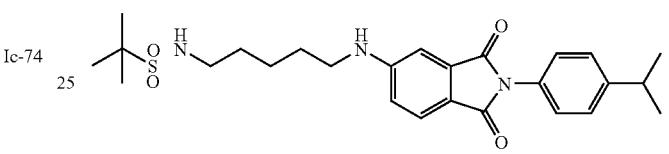
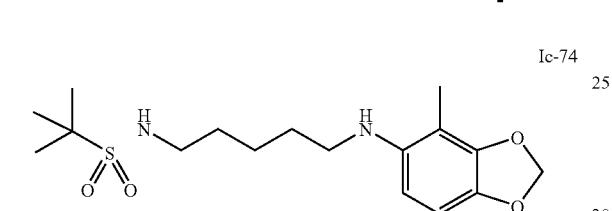
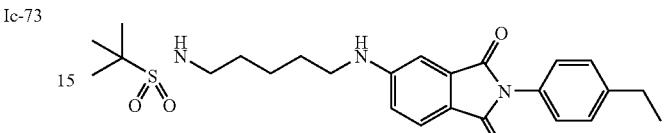
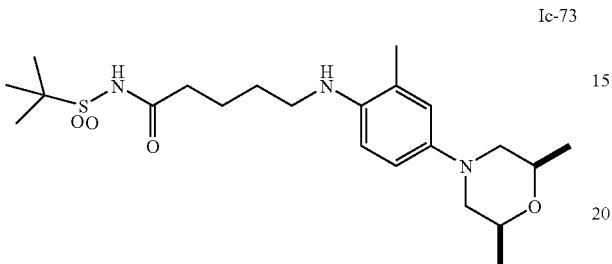
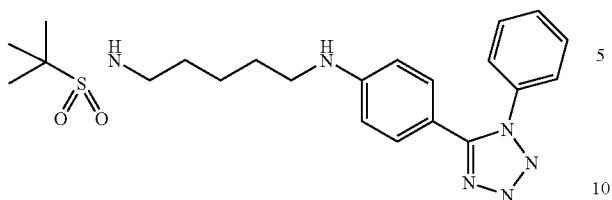
Ic-64



233

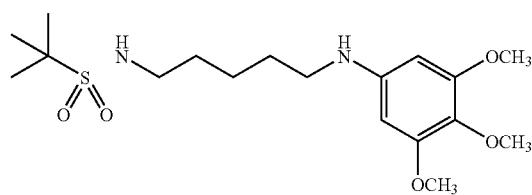


234



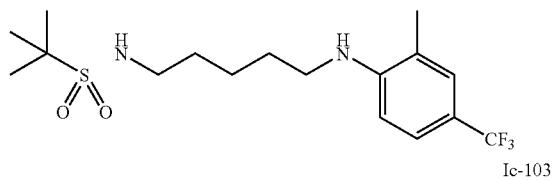
237
-continued

Ic-101

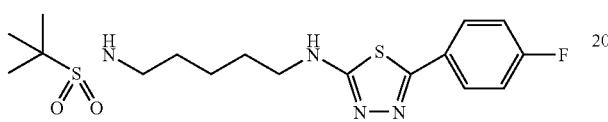


Ic-102

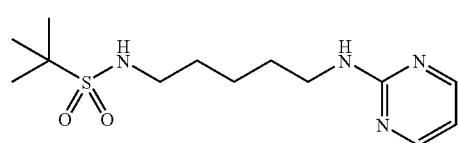
[Formula 130]



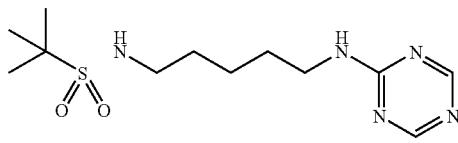
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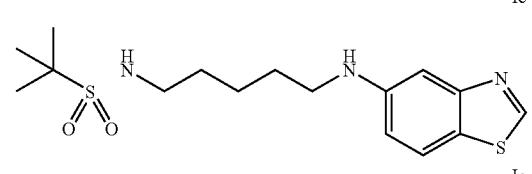
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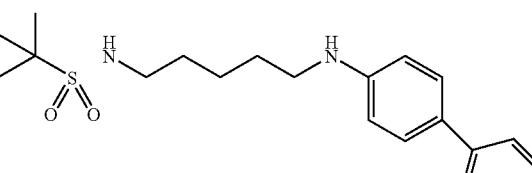
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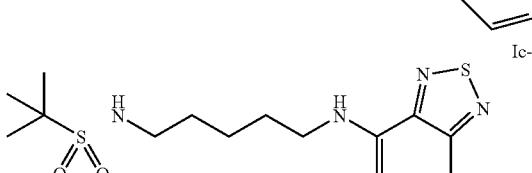
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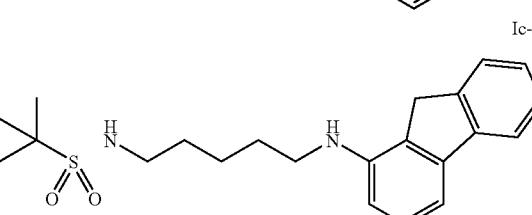
35



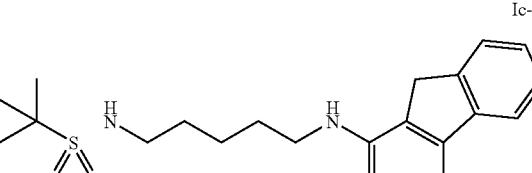
40



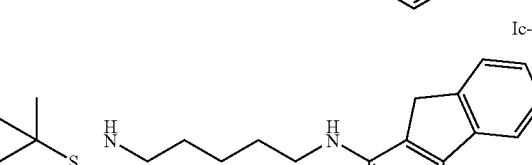
45



50



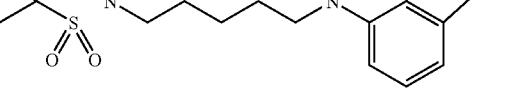
55



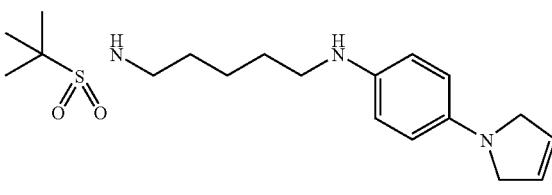
60



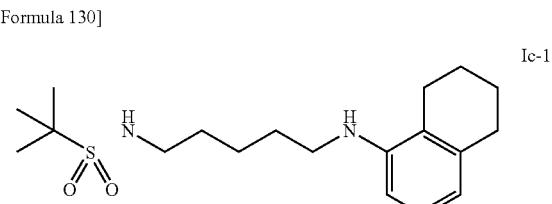
65

**238**
-continued

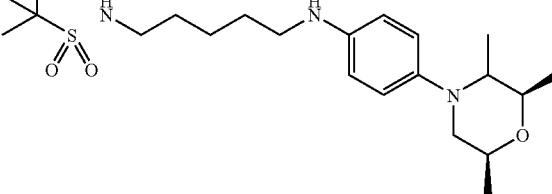
Ic-110



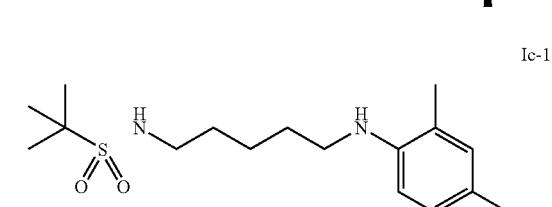
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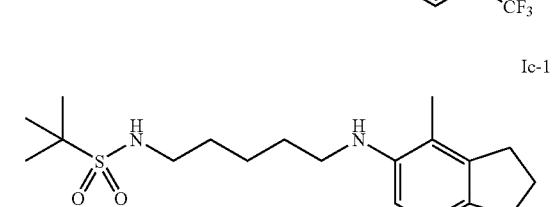
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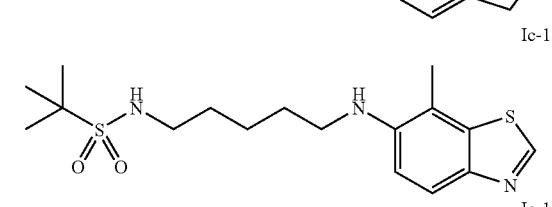
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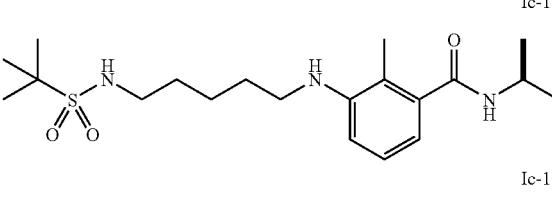
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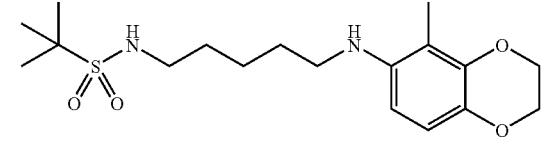
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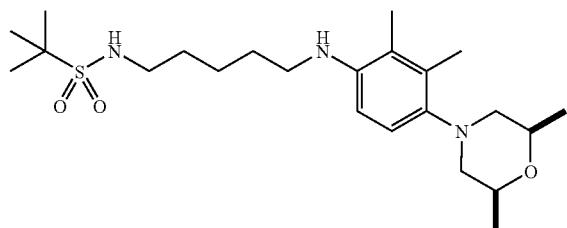


50

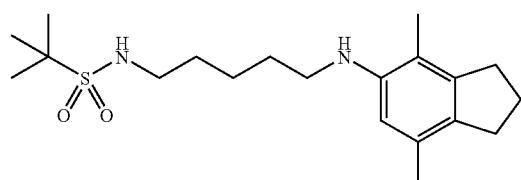
239

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Ic-118

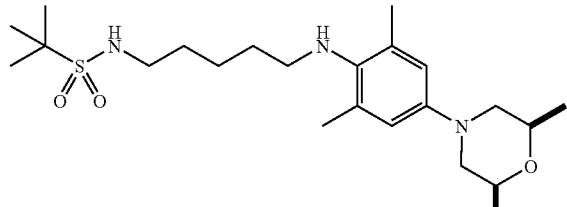
10
15

Ic-119



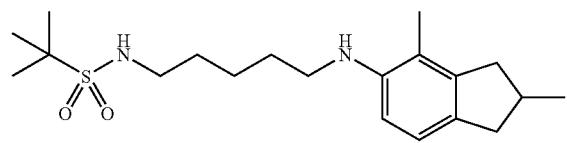
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Ic-120



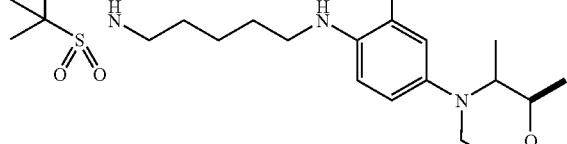
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Ic-121



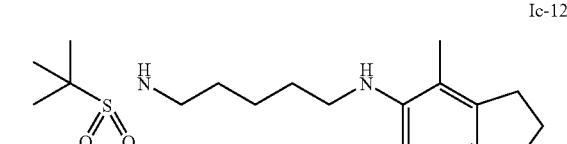
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Ic-122



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Ic-123



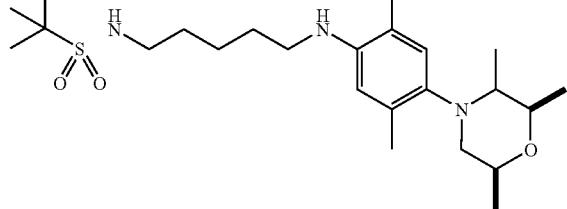
40

Ic-124



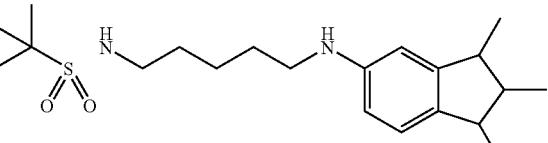
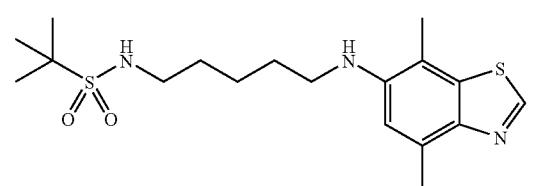
45

Ic-125

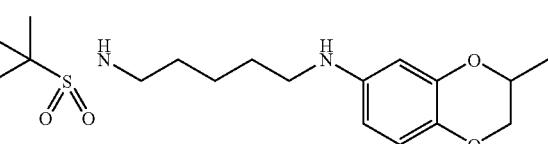


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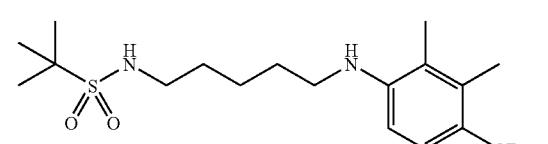
Ic-126

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10

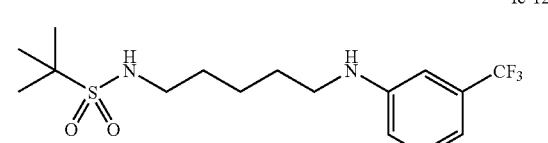
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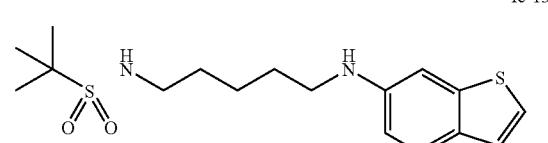
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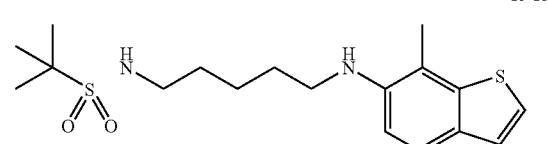
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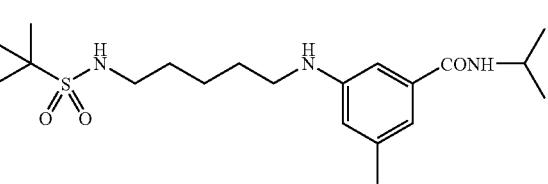
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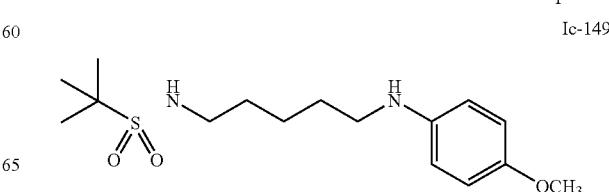
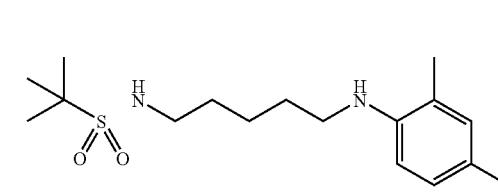
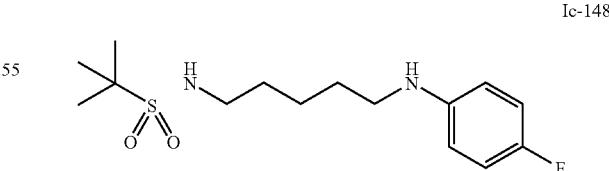
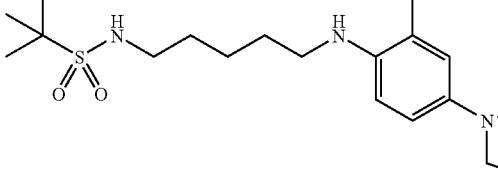
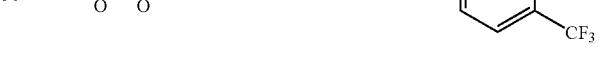
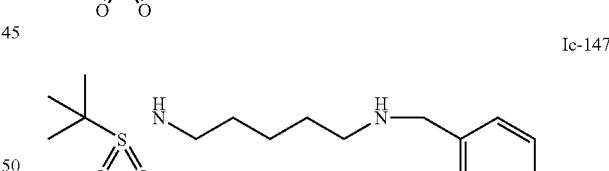
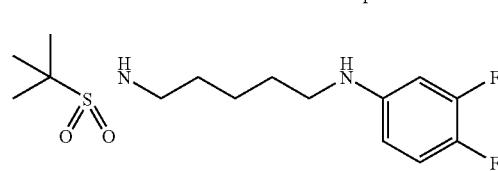
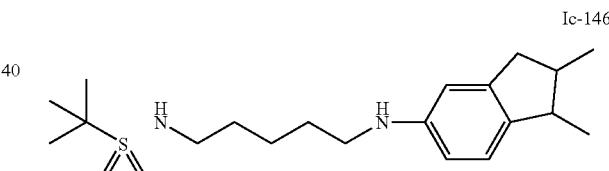
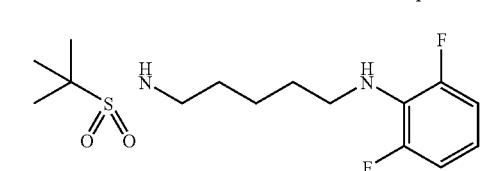
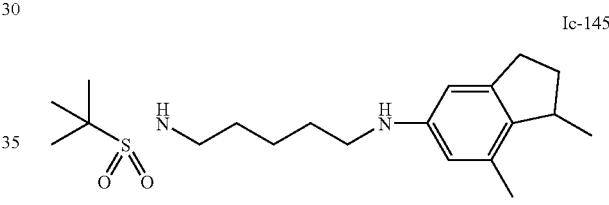
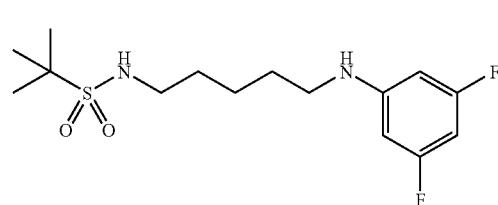
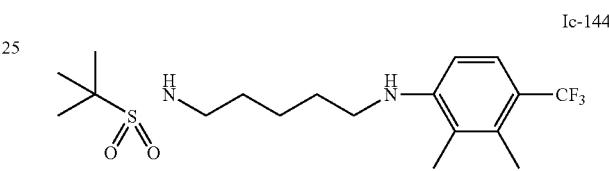
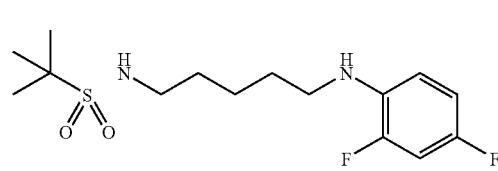
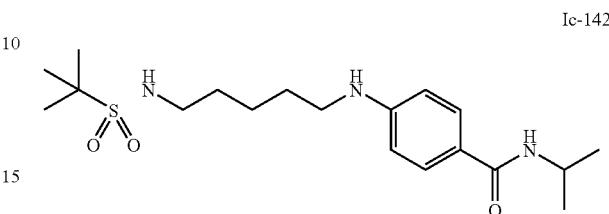
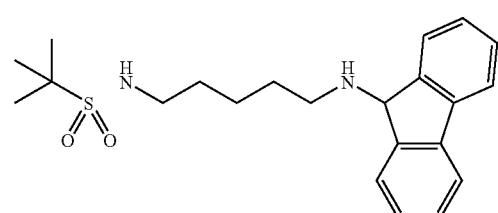
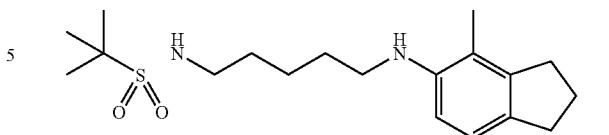
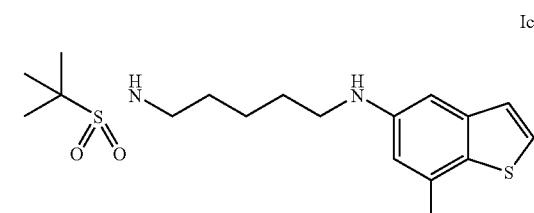


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241

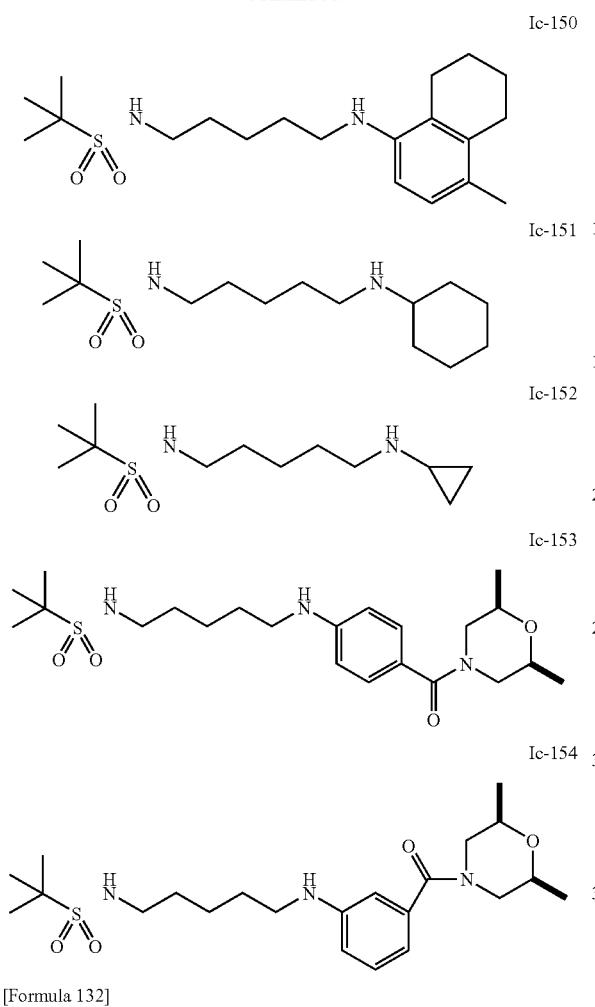
-continued

[Formula 131]



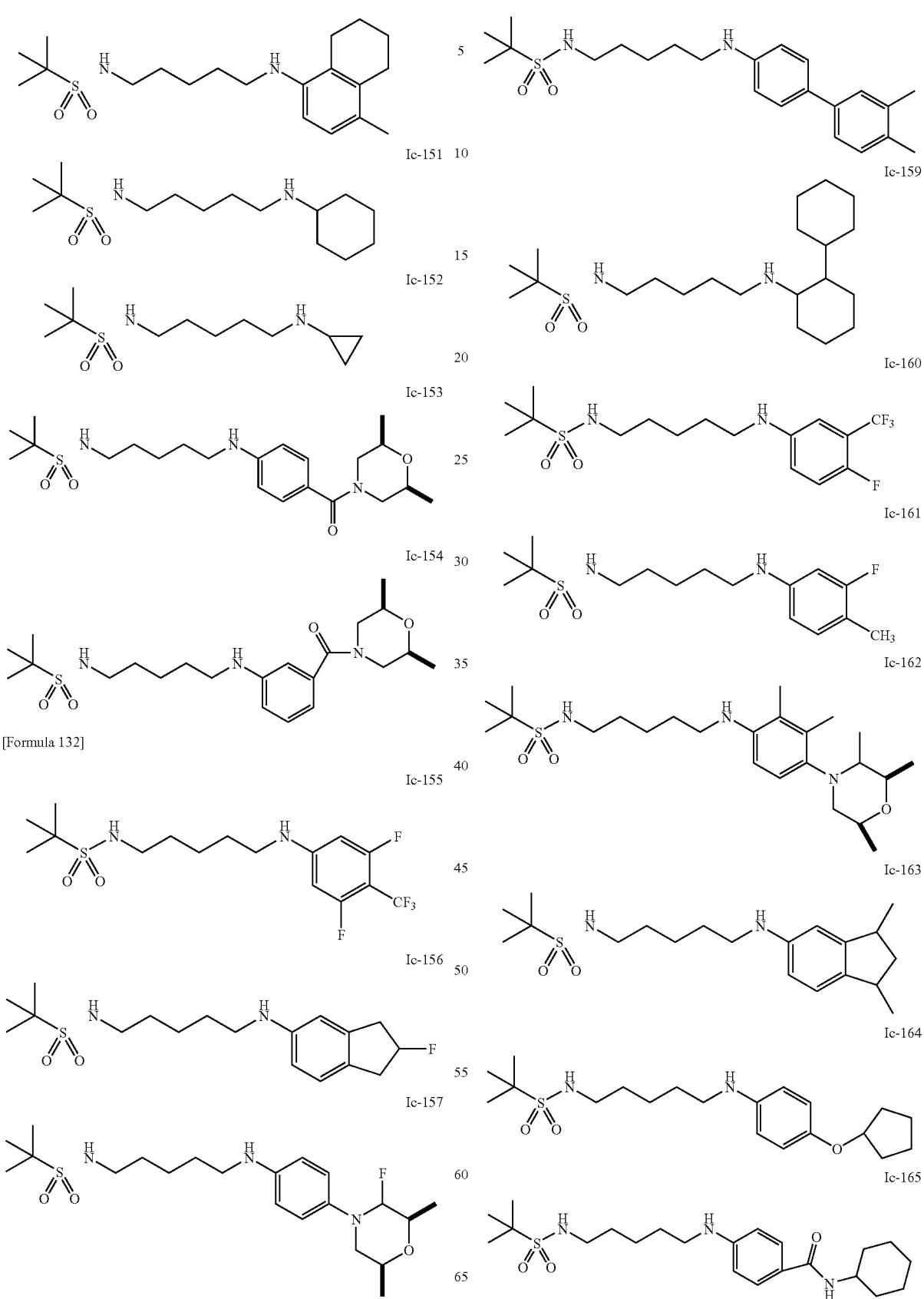
243

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**244**

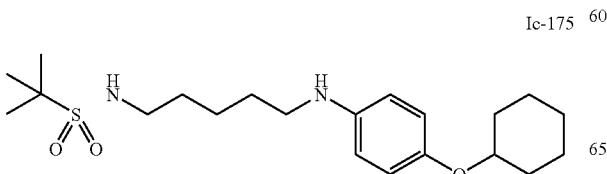
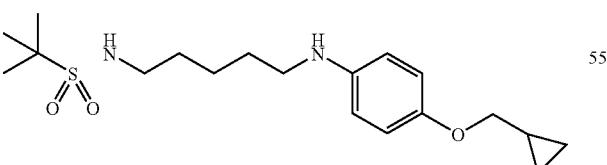
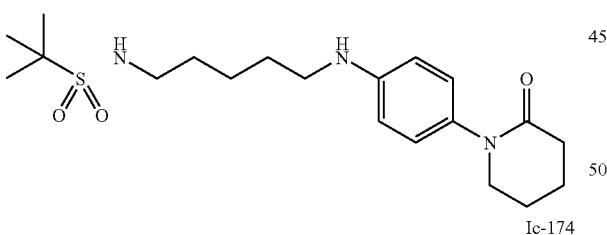
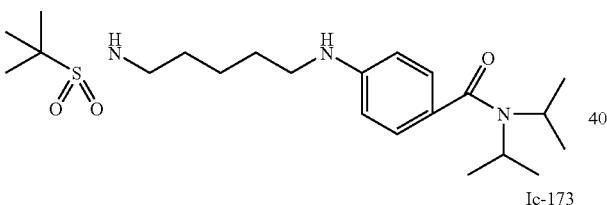
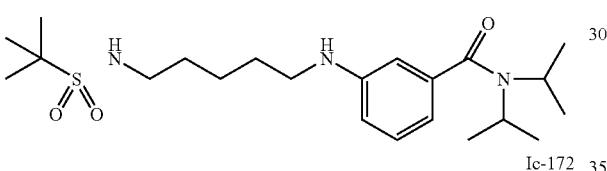
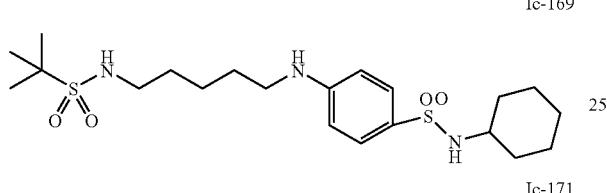
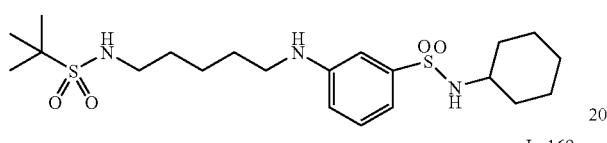
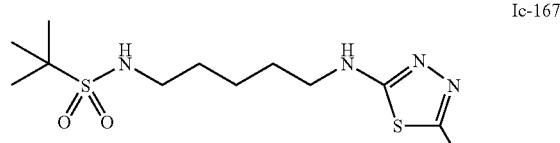
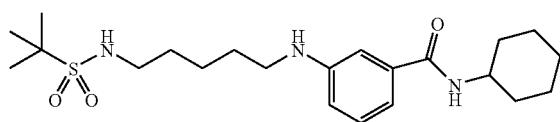
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Ic-158



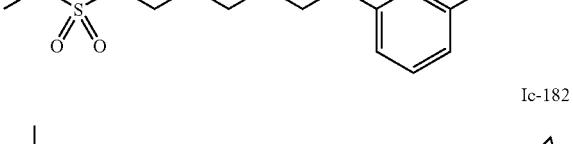
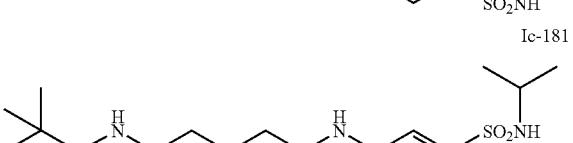
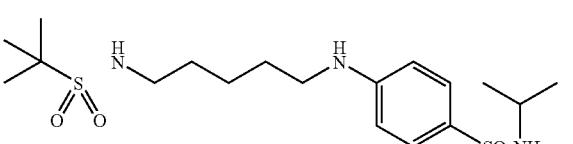
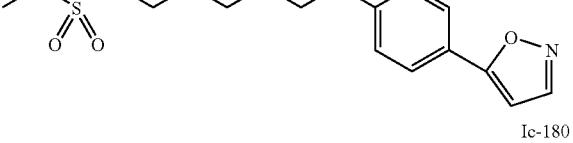
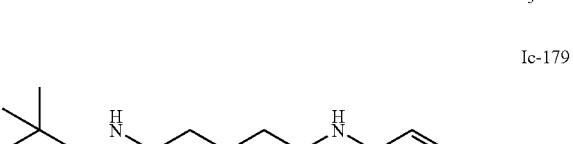
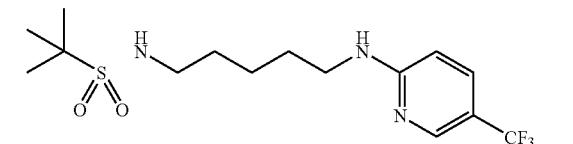
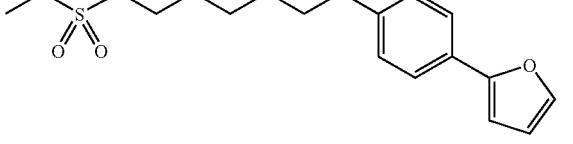
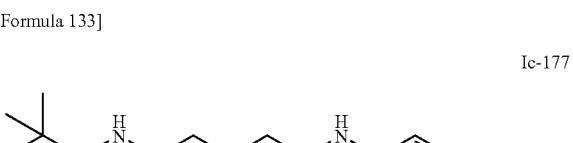
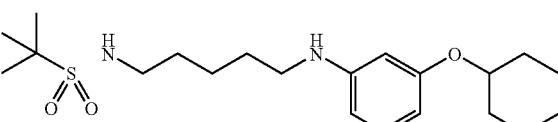
245

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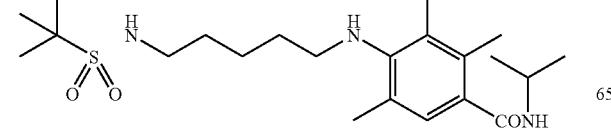
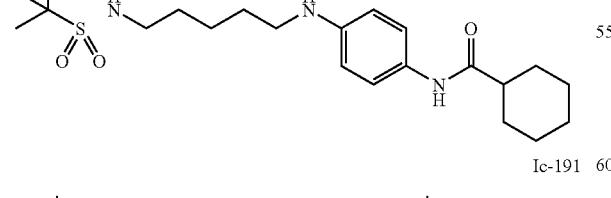
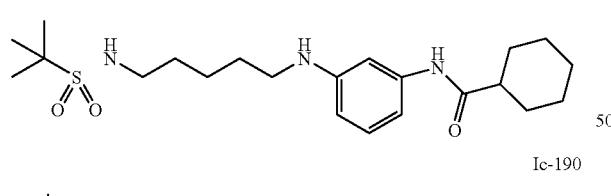
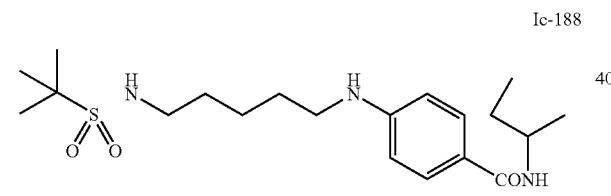
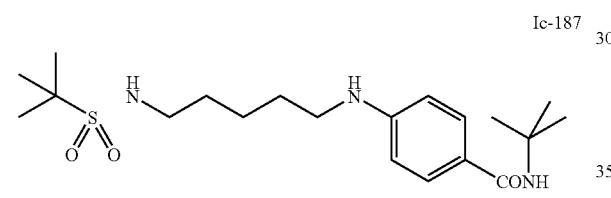
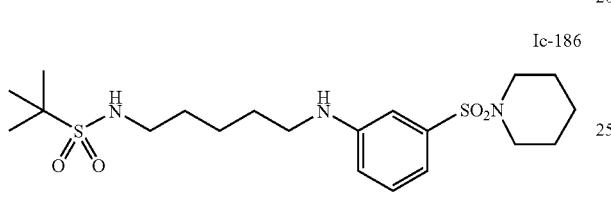
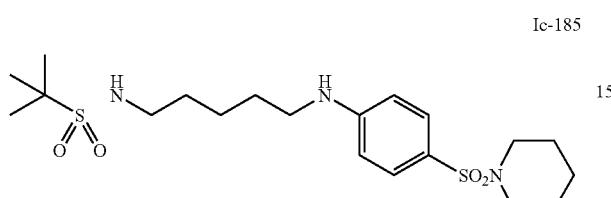
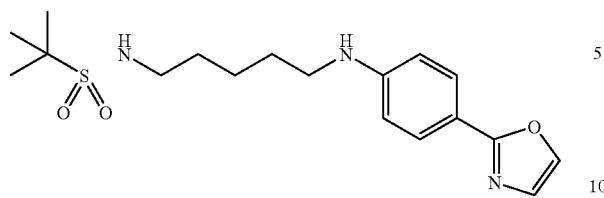
**246**

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Ic-176

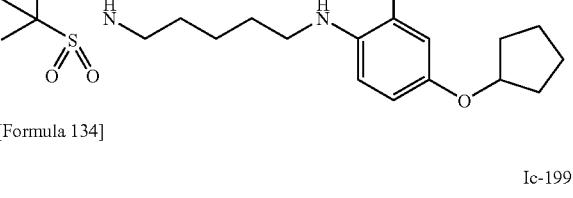
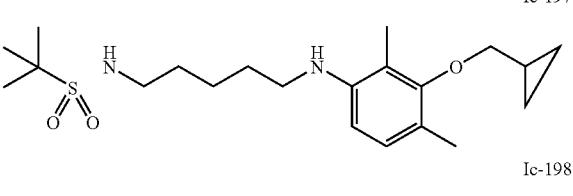
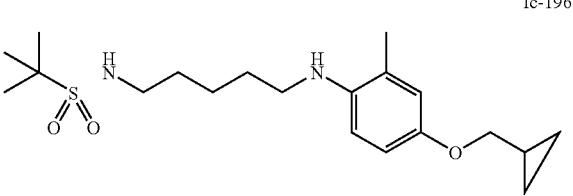
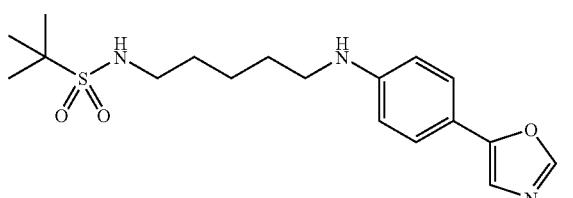
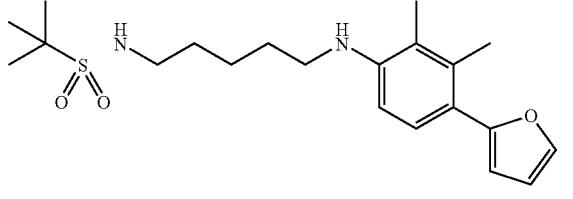
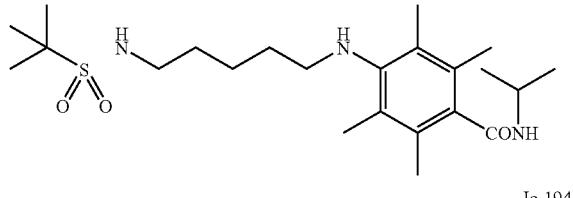
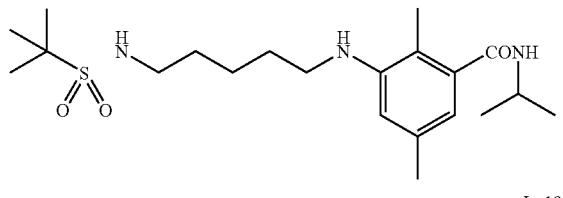


247
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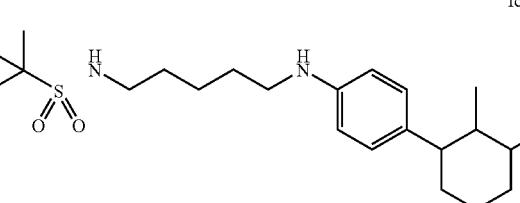
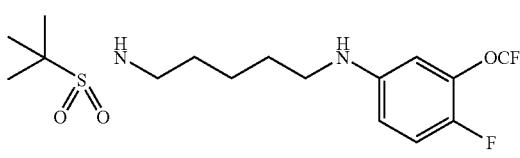
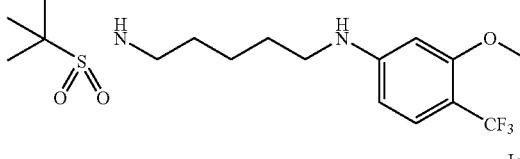
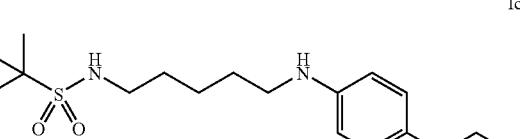
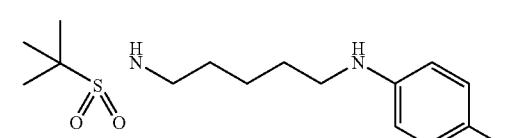
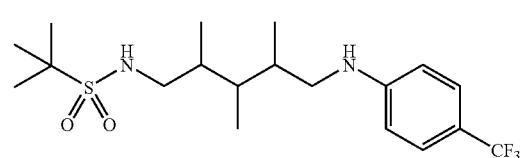
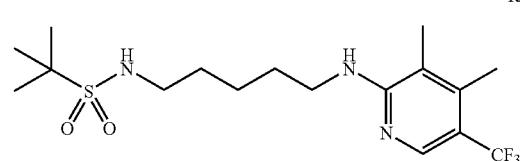
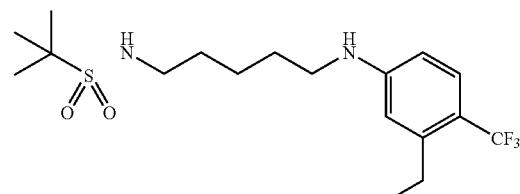
248
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Ic-192

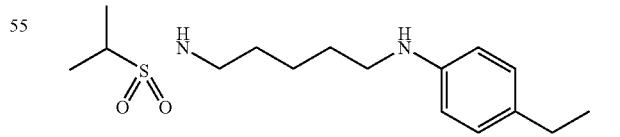
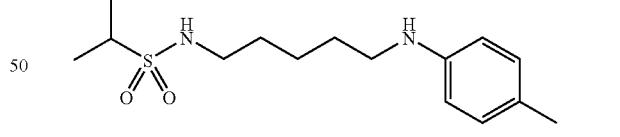
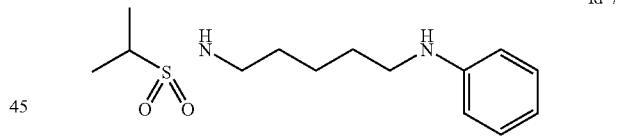
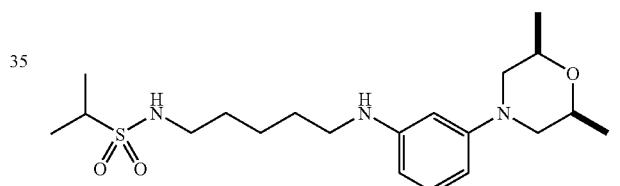
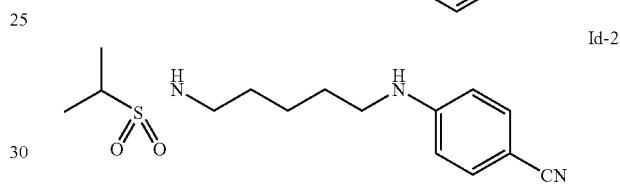
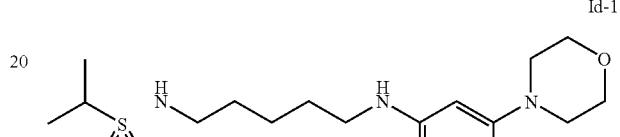
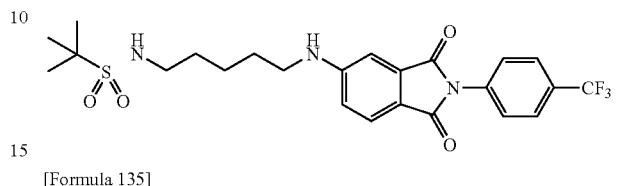
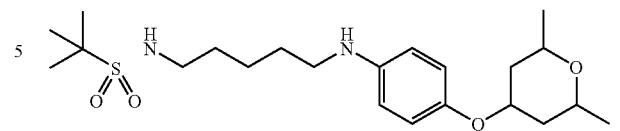


251

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**252**

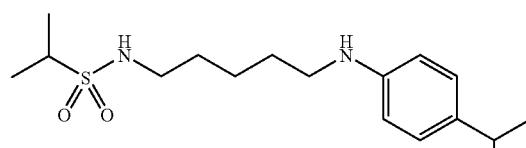
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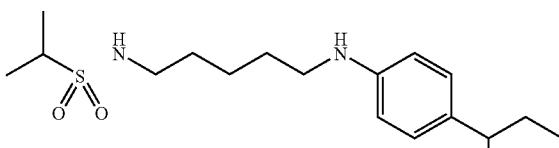
253

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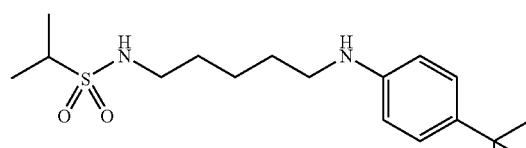
Id-11



Id-12 10

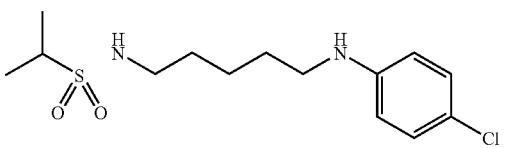


Id-13 15

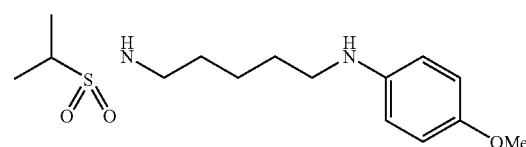


Id-14 20

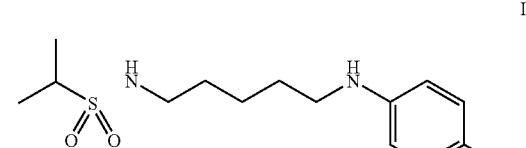
[Formula 136]



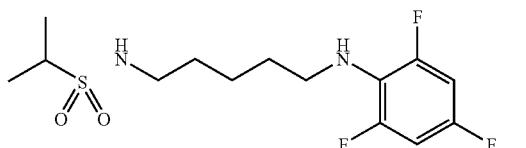
Id-16 30



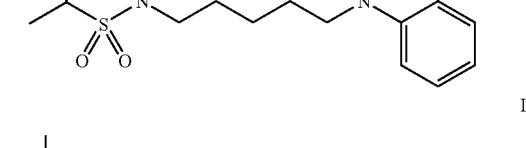
Id-17 35



Id-18 45



Id-19 55

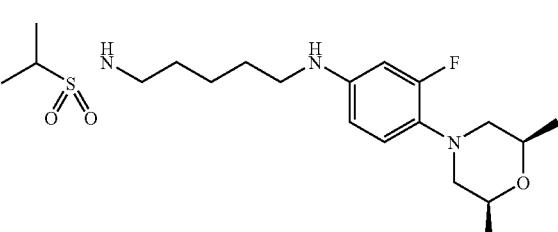


Id-20 60

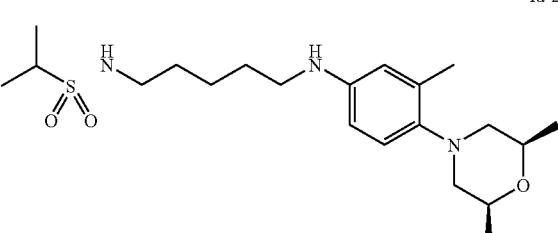
254

-continued

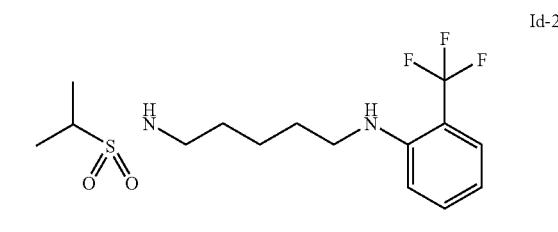
Id-21



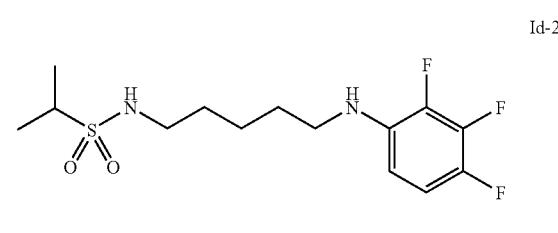
Id-22 15



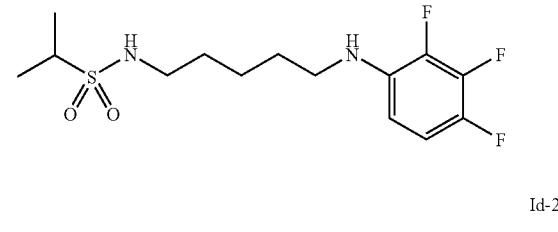
Id-14 20



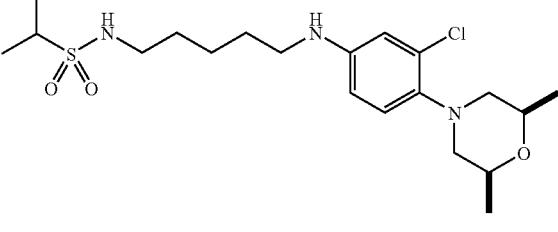
Id-16 30



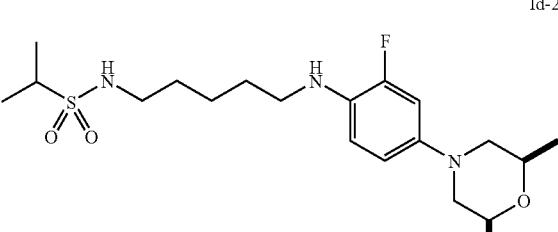
Id-17 40



Id-18 45



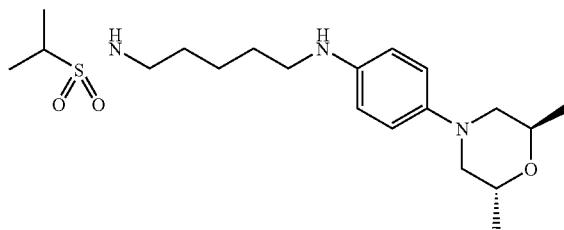
Id-19 55



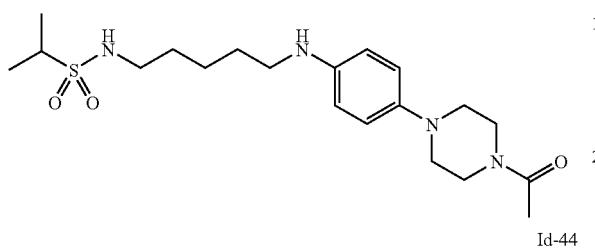
Id-20 65

257

-continued

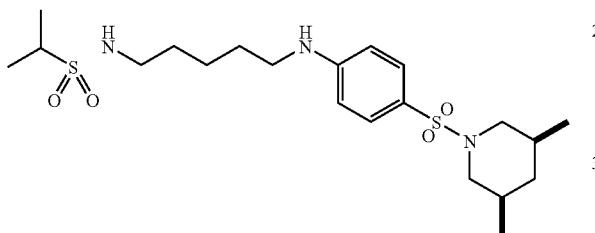


Id-43



15

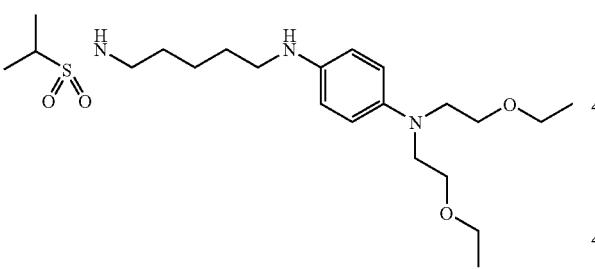
Id-44



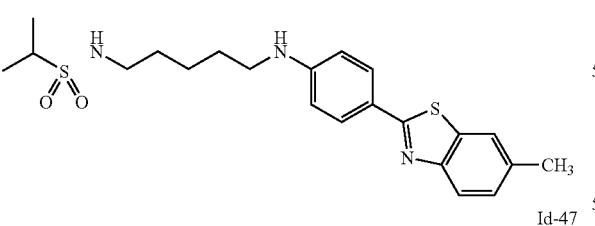
Id-45

35

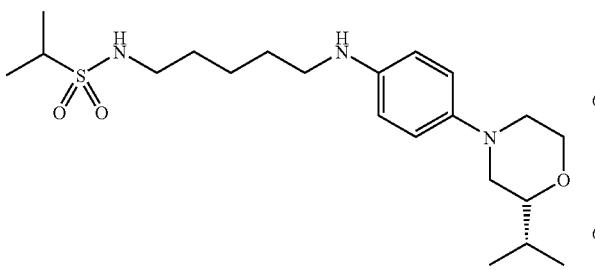
Id-46



Id-46



Id-47

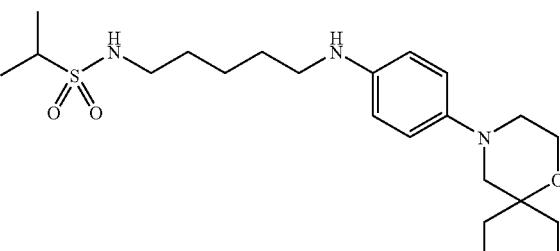


Id-48

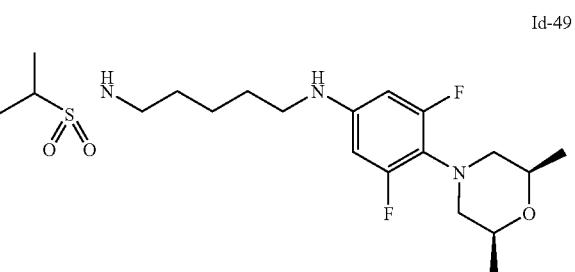
258

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Id-48



Id-43



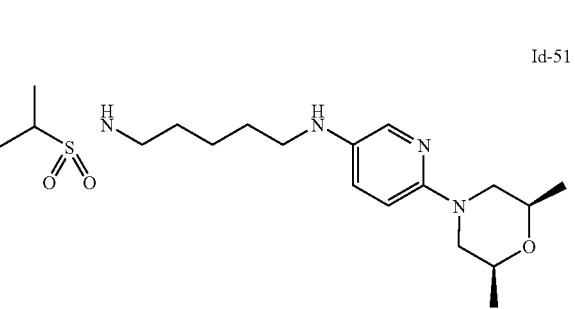
Id-44

15

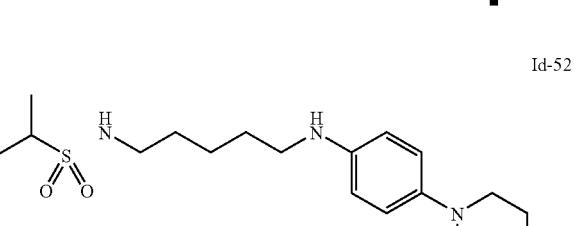
Id-45

35

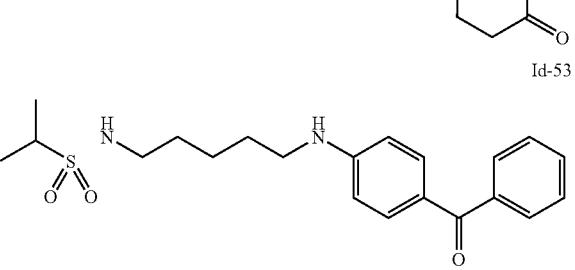
Id-46



Id-46



Id-47

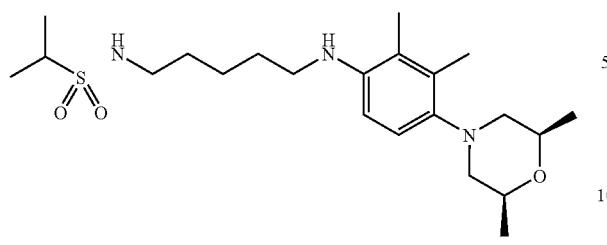


Id-48

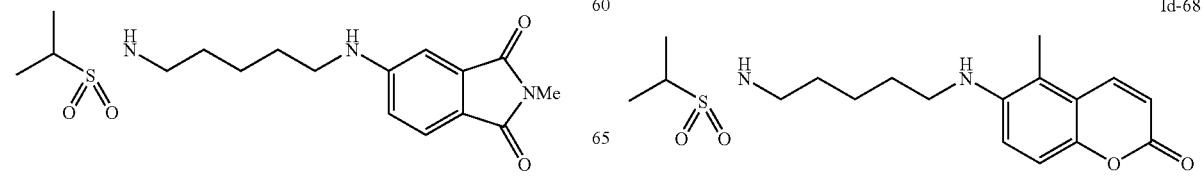
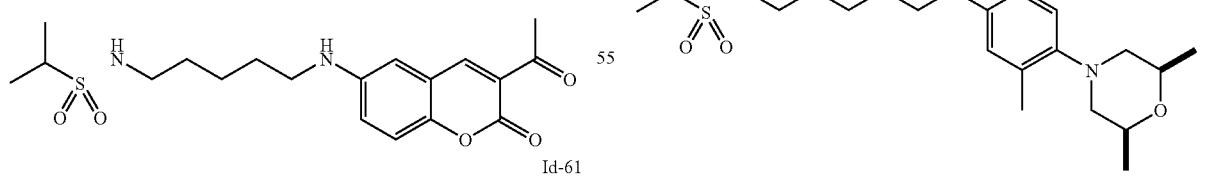
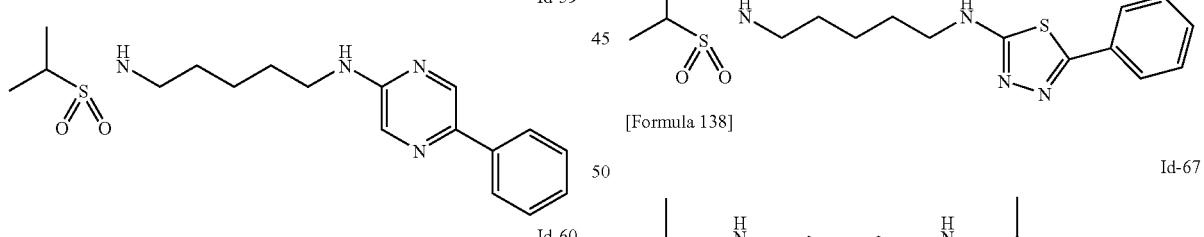
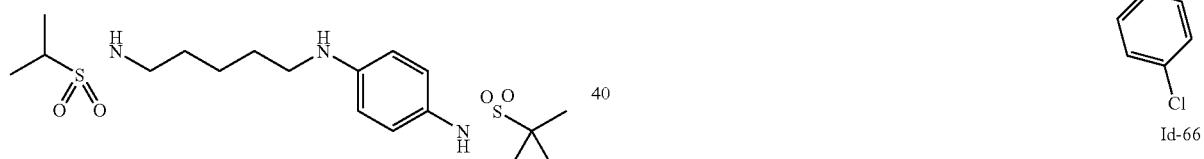
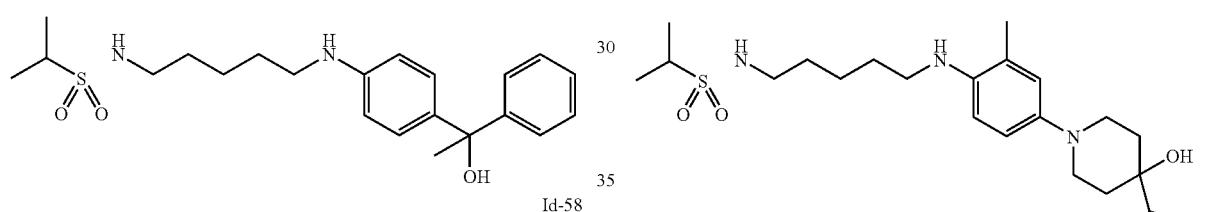
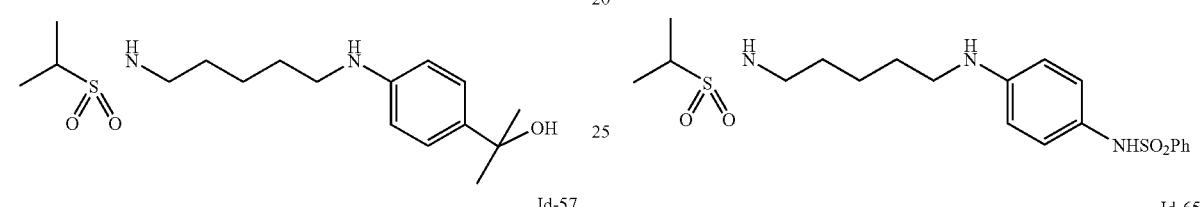
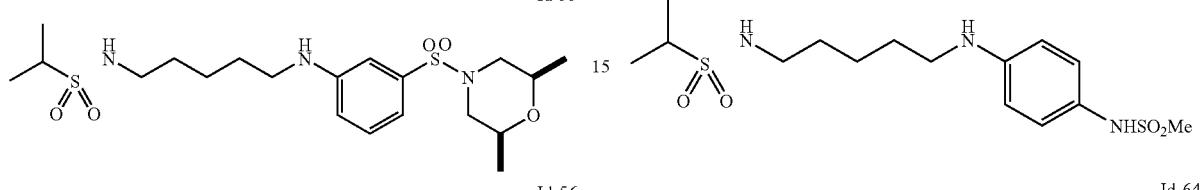
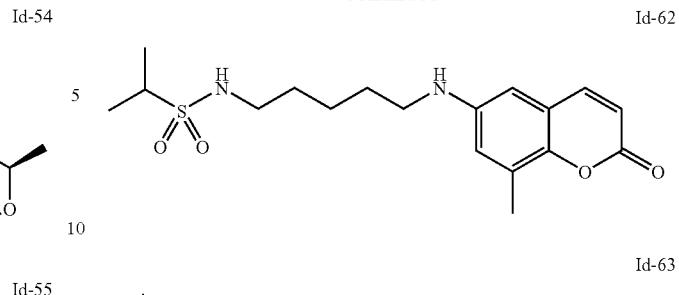
[Formula 137]

259

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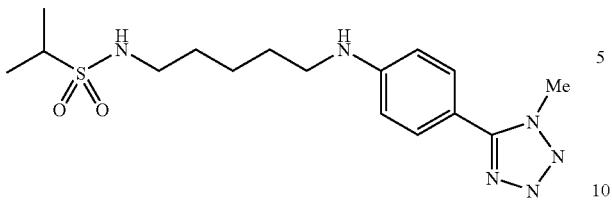
**260**

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261

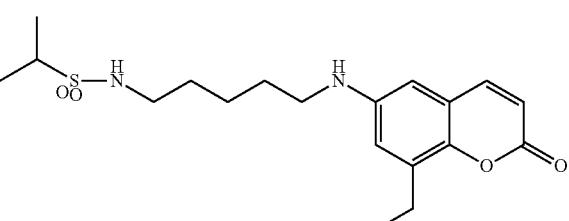
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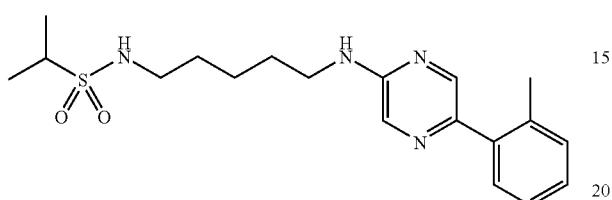
Id-69

262

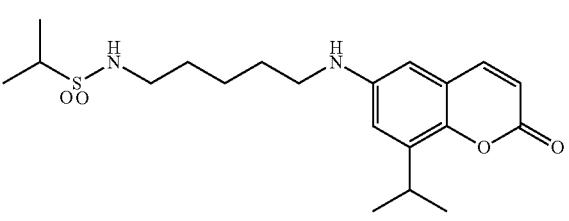
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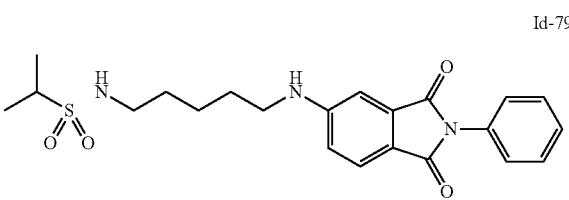
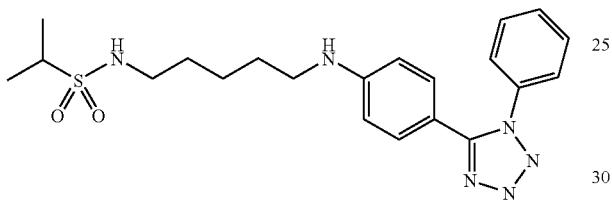
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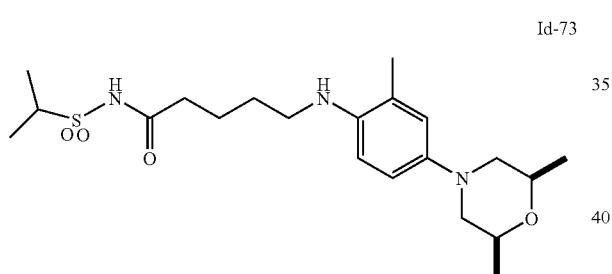
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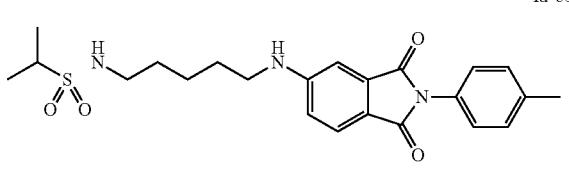
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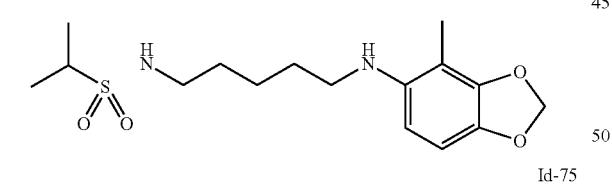
JJ 90



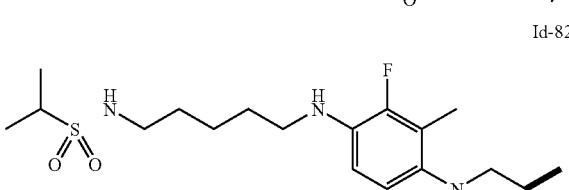
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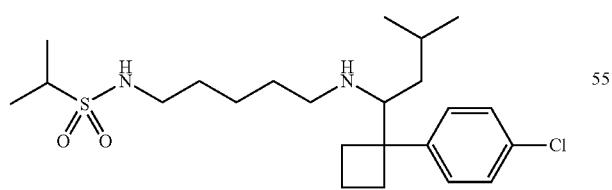
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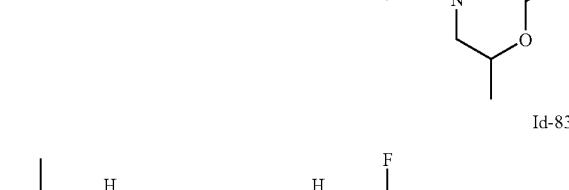
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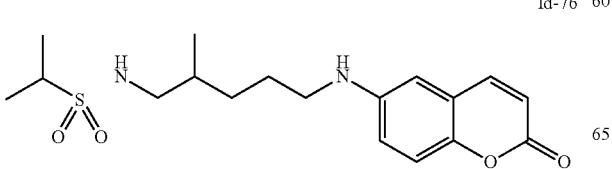
Id-82



176



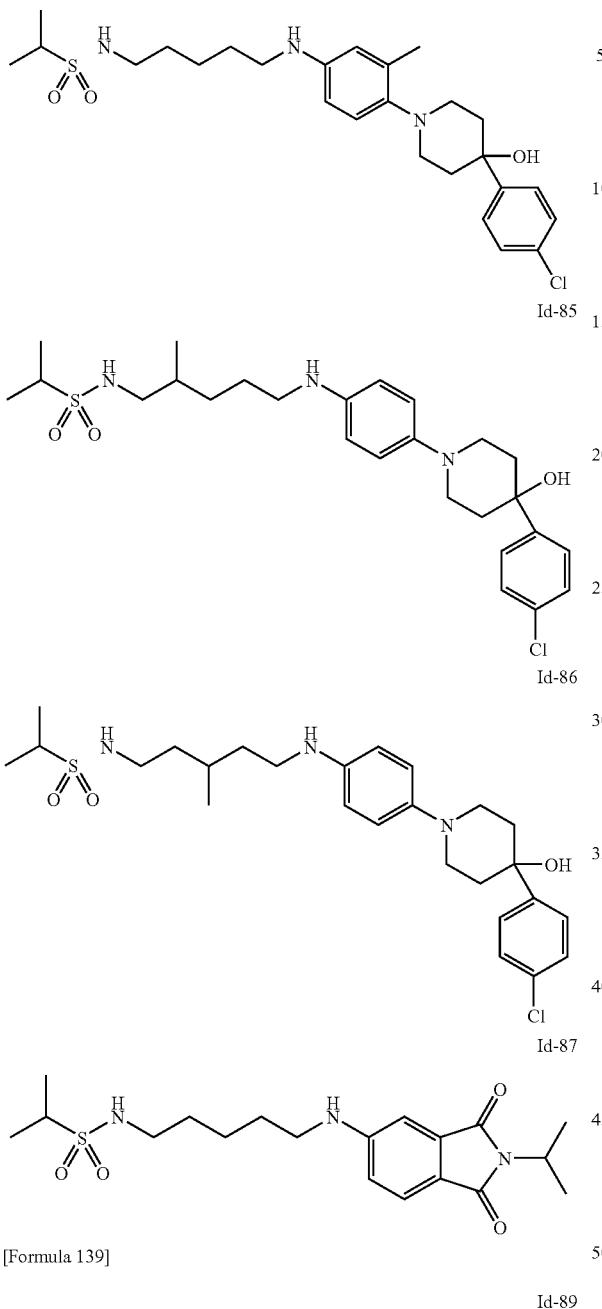
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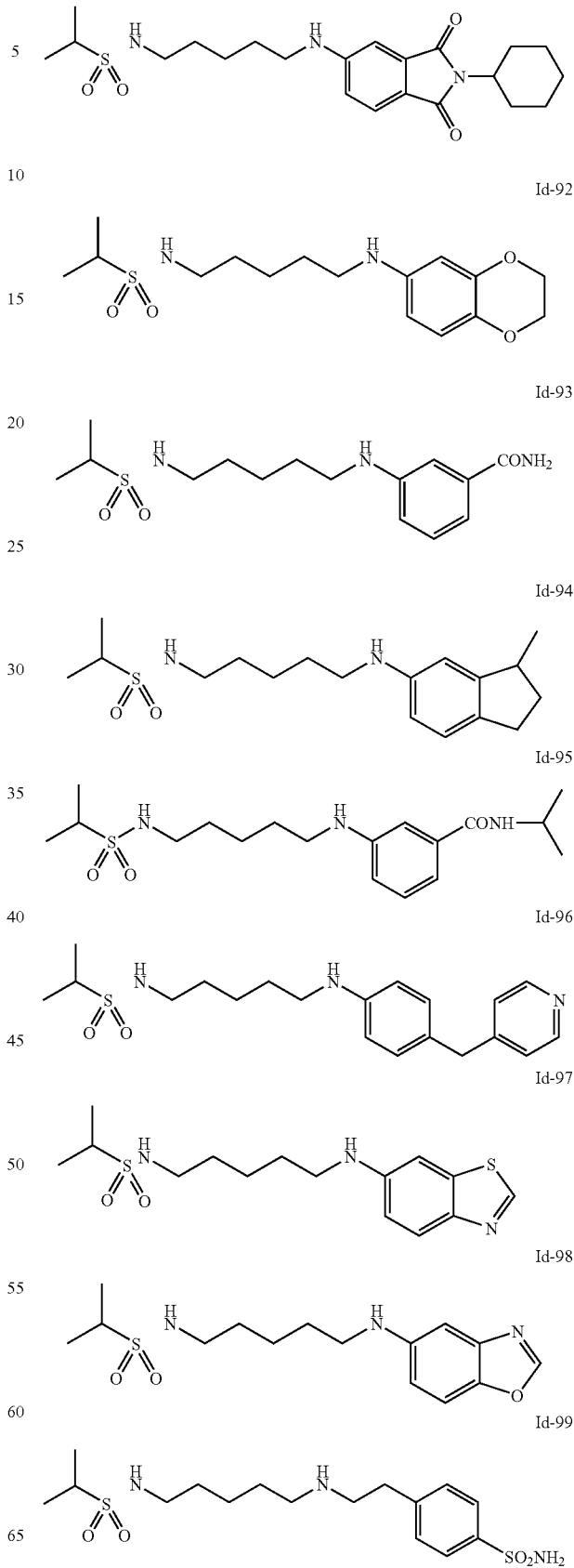
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263

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**264**

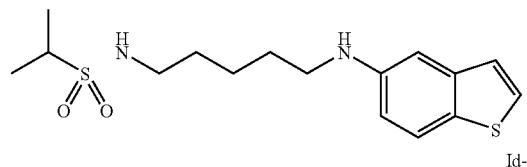
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265

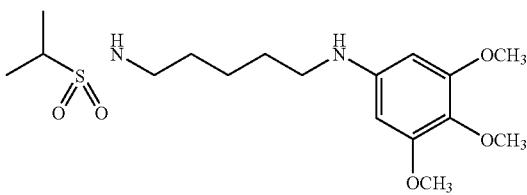
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Id-100



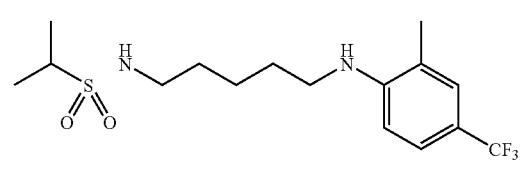
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Id-101



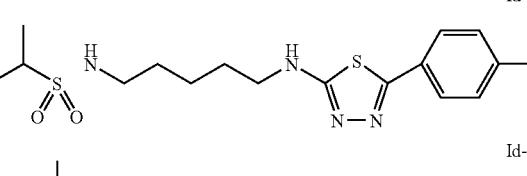
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Id-102



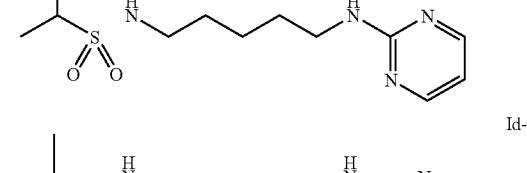
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Id-103



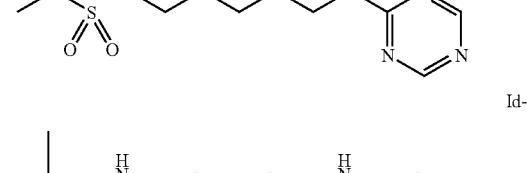
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Id-104



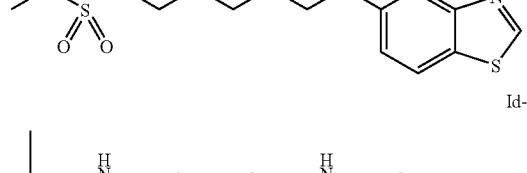
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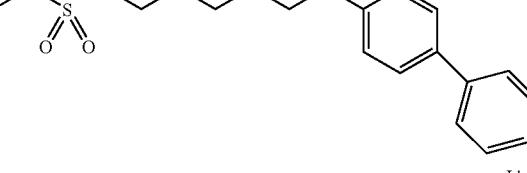
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Id-106



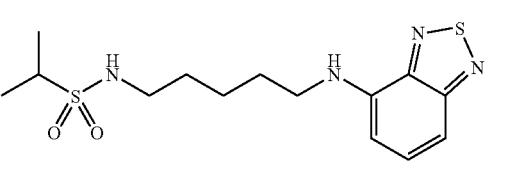
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Id-107



45

Id-108



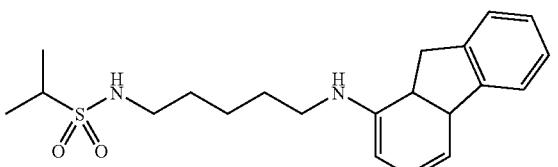
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Id-109

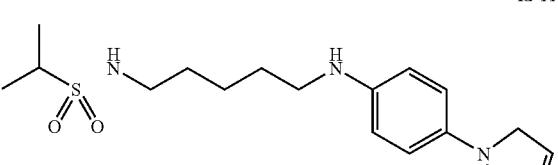
**266**

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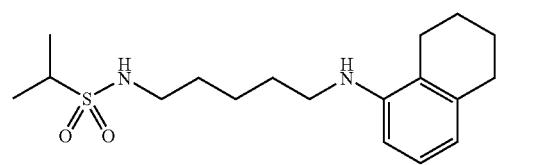
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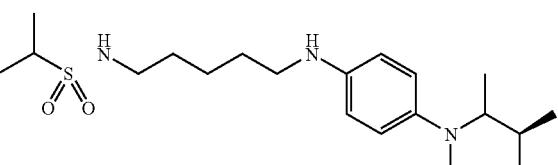
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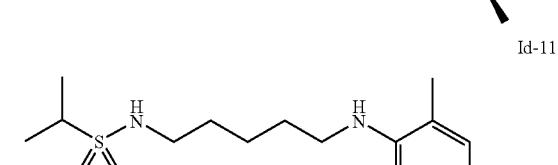
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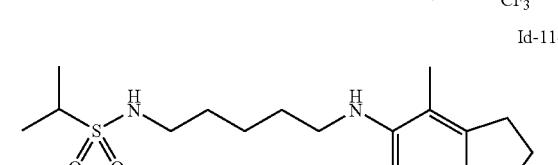
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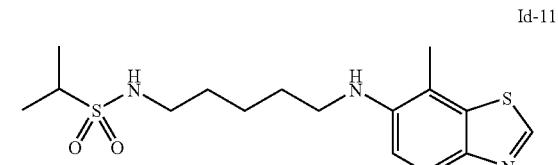
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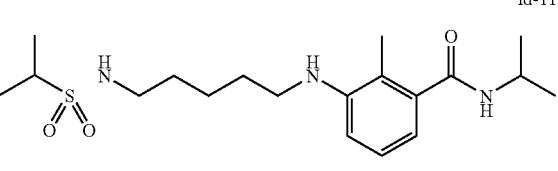
Id-114



Id-115



Id-116

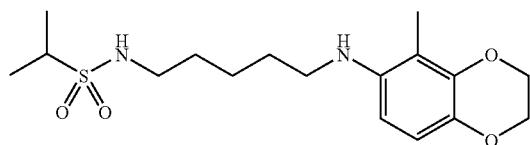


Id-117

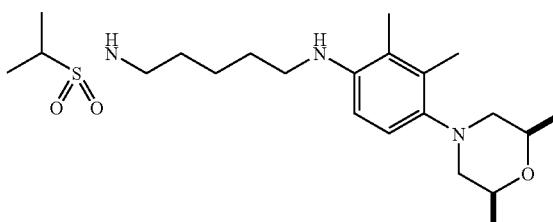
267

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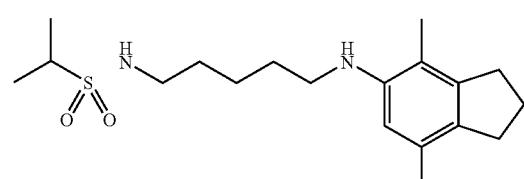
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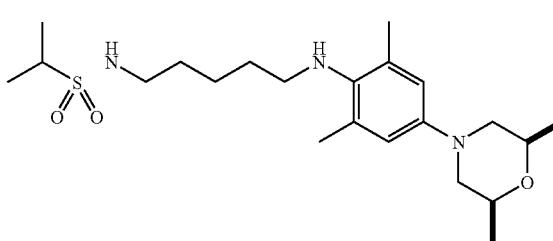
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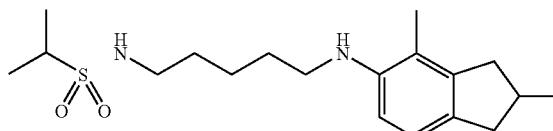
Id-119



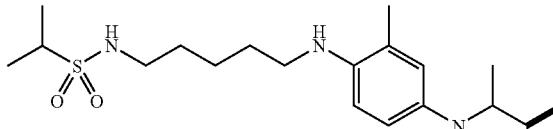
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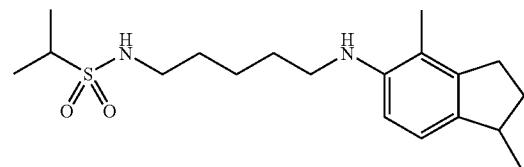
Id-121



Id-122



Id-123

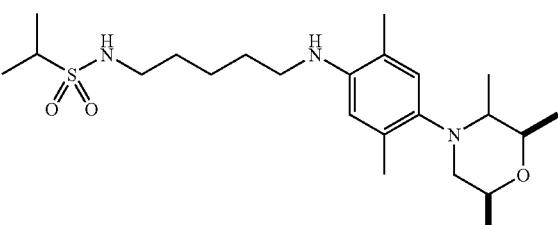


Id-124

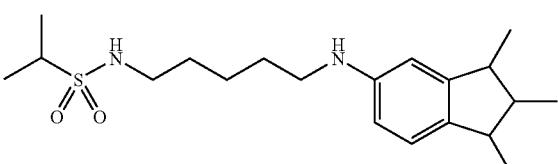
268

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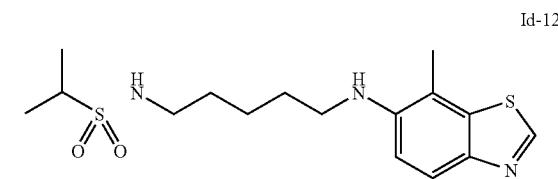
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Id-125

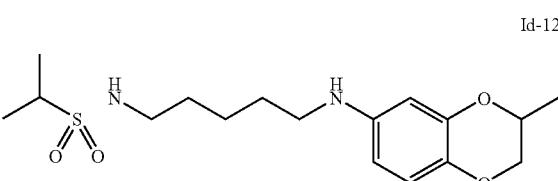


Id-119



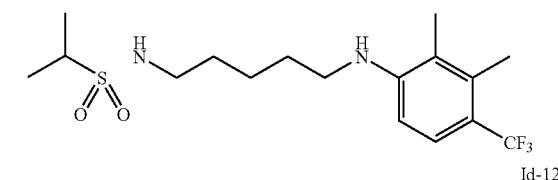
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Id-120



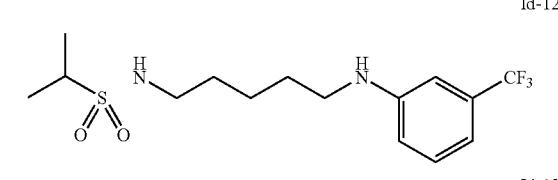
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Id-120



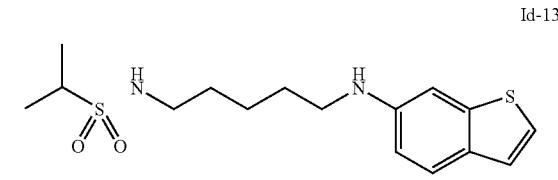
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Id-121



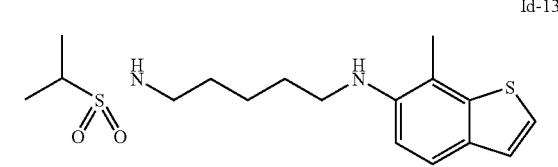
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Id-122



Id-130

Id-123

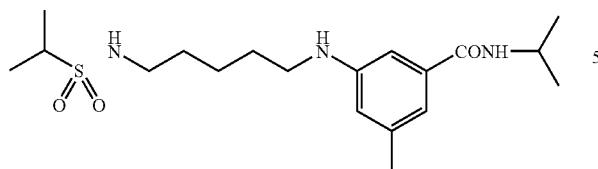


Id-131

269

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Id-132



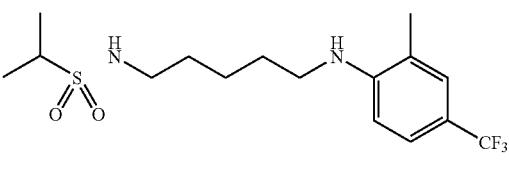
[Formula 141]

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270

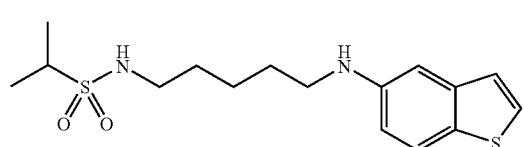
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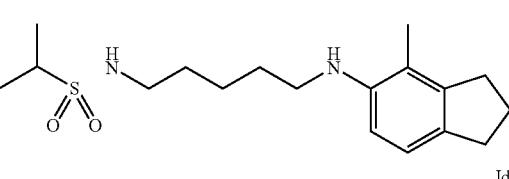


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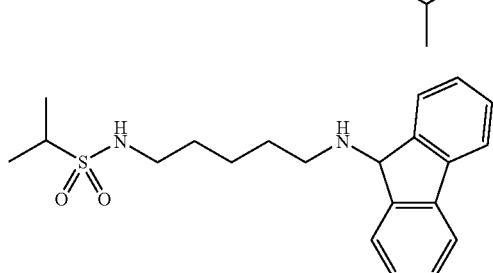
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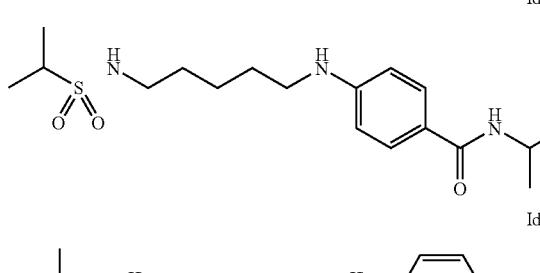
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Id-142

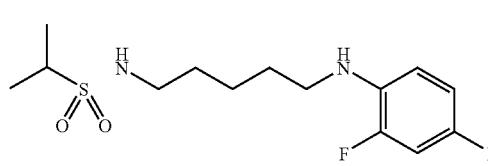


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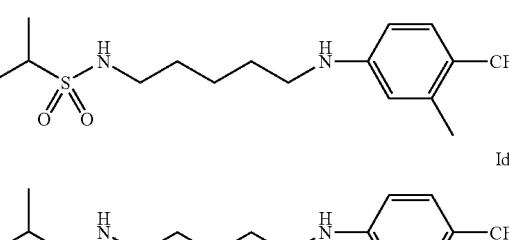


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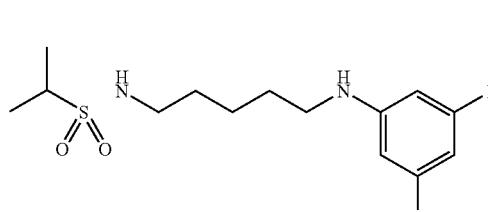
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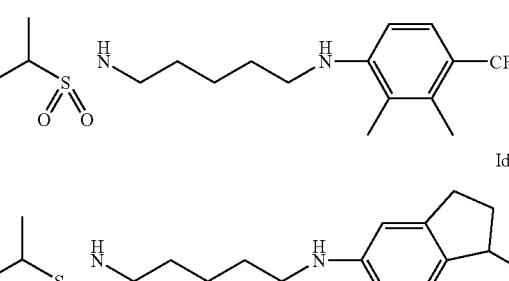
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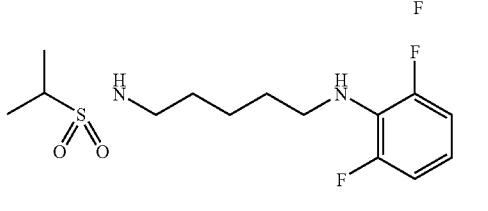
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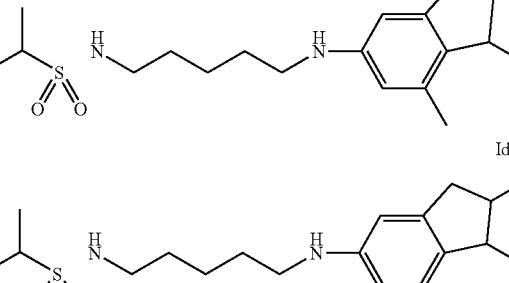
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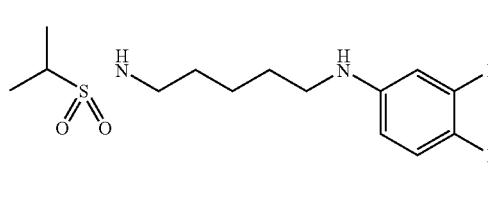
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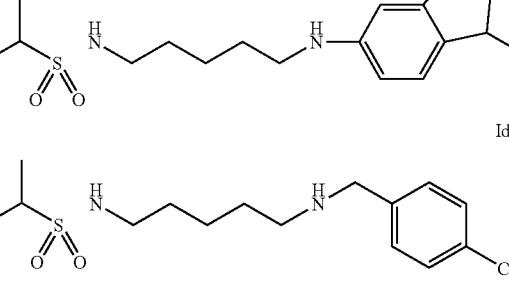
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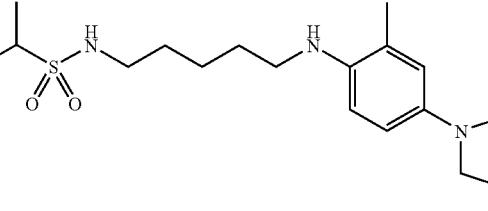
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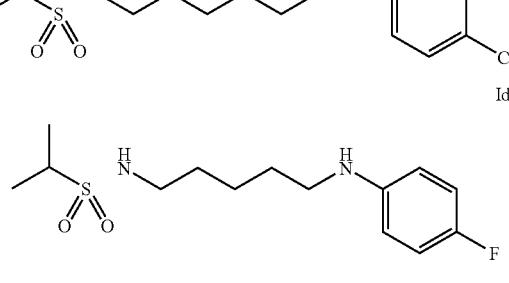
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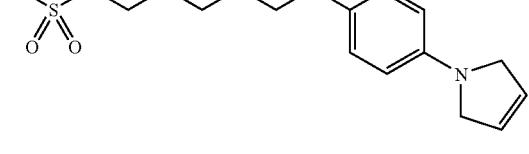


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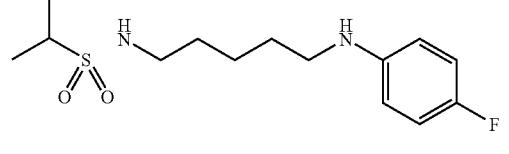


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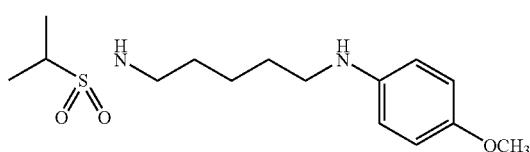
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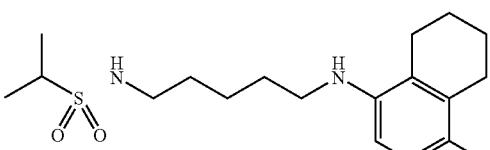
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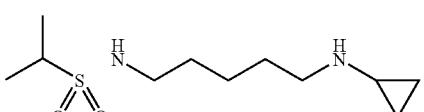
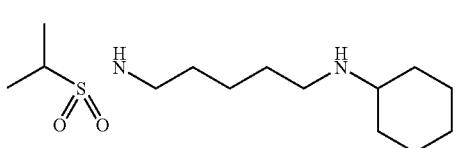
271



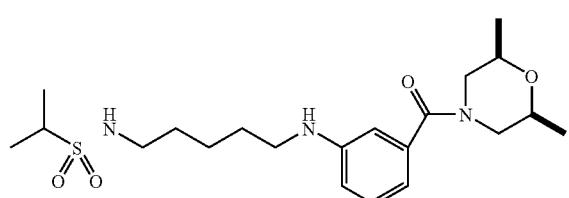
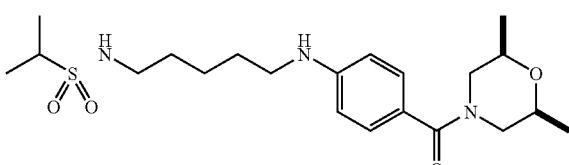
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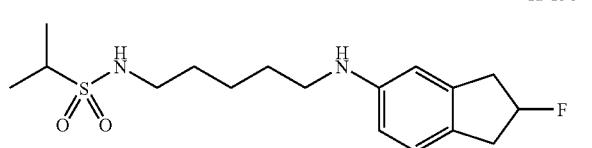
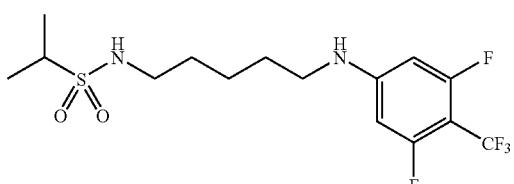
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25

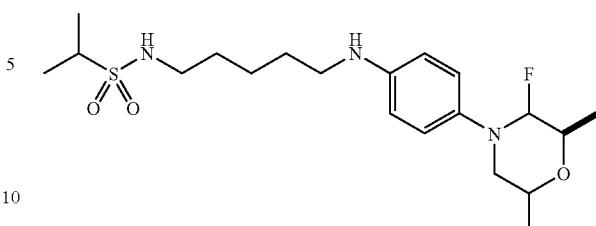


[Formula 142]

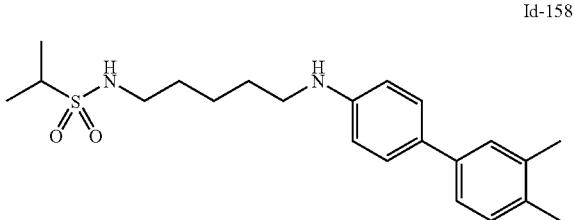


Id-156 60

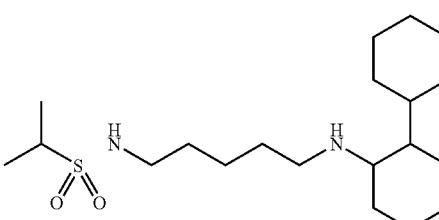
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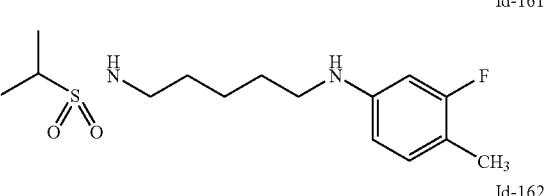
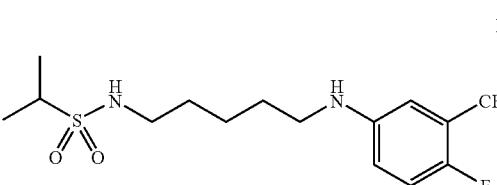
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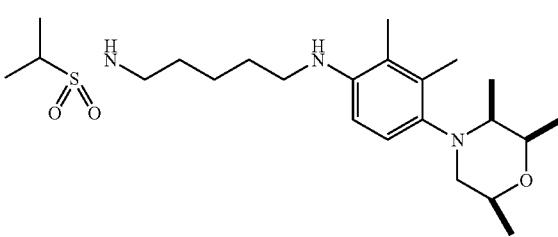
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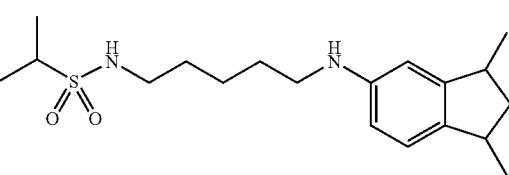
Id-159



Id. 161



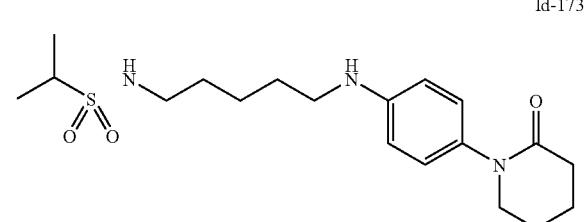
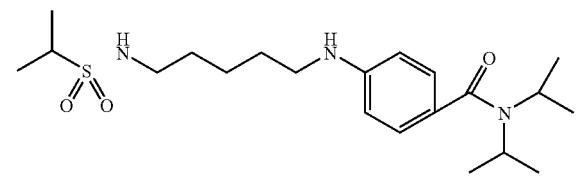
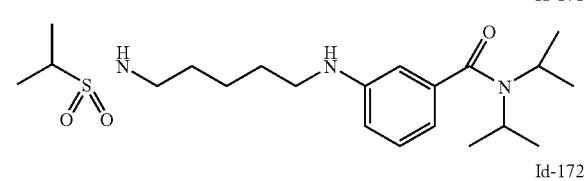
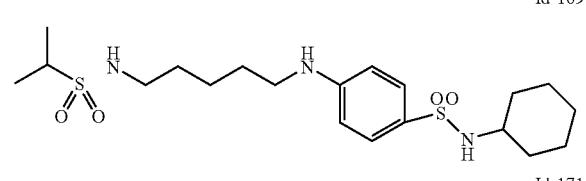
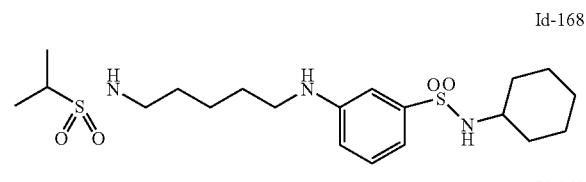
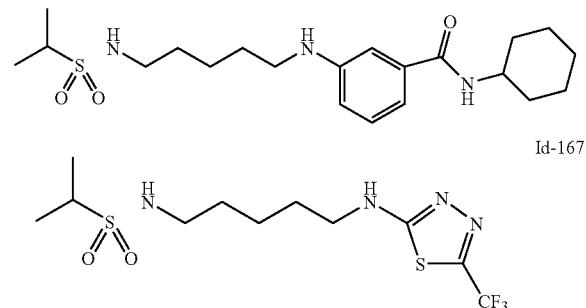
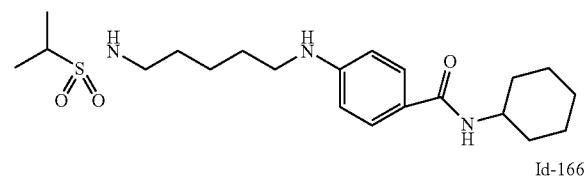
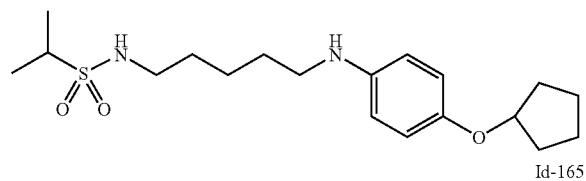
J-163



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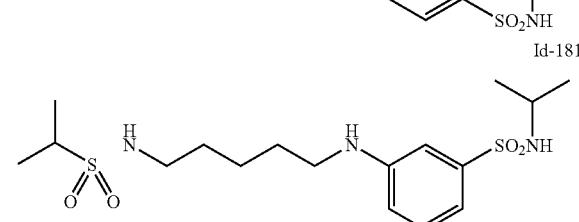
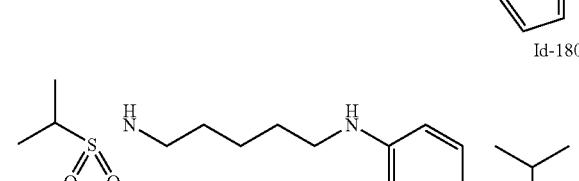
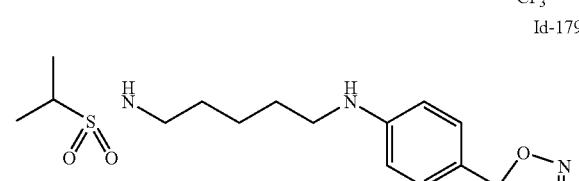
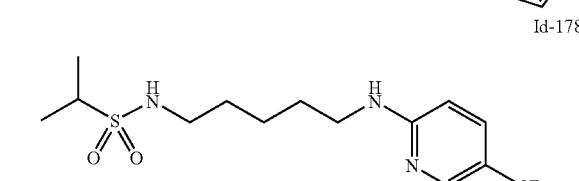
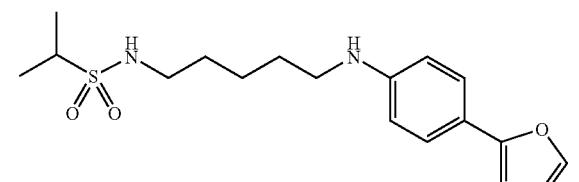
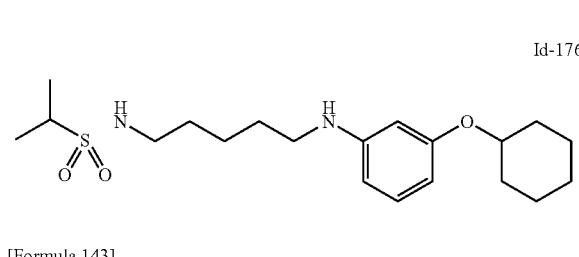
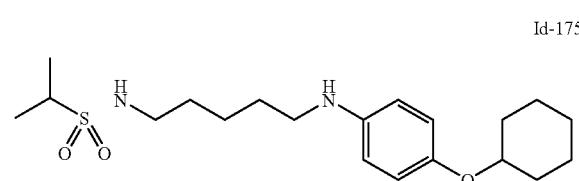
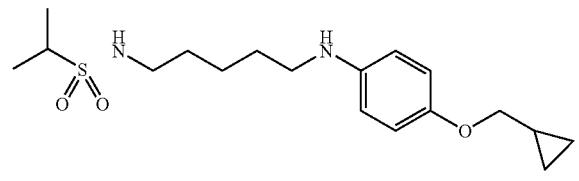
273

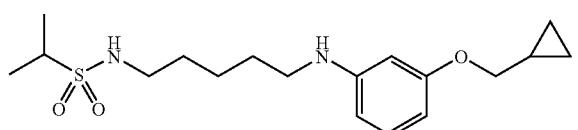
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**274**

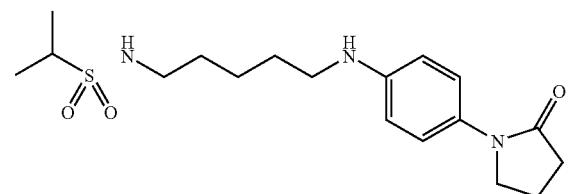
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Id-174

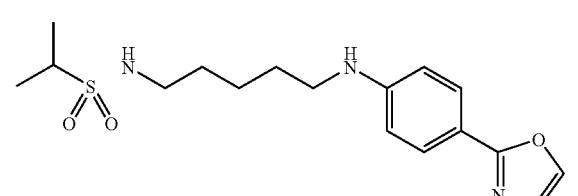


275
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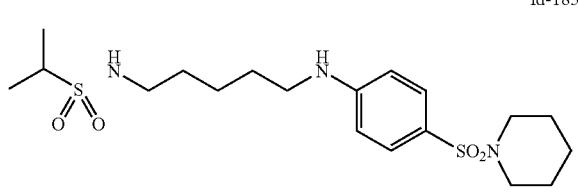
5 Id-183 10



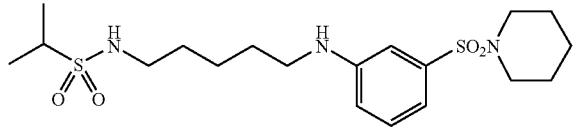
15 Id-184 20



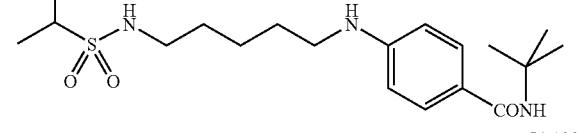
25 Id-185 30



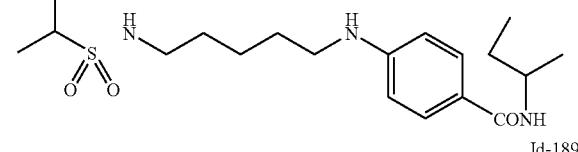
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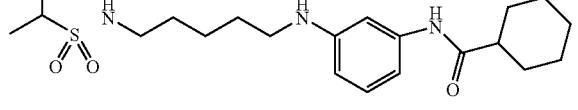
45 Id-187



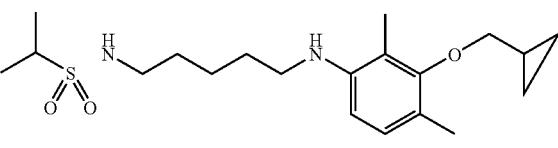
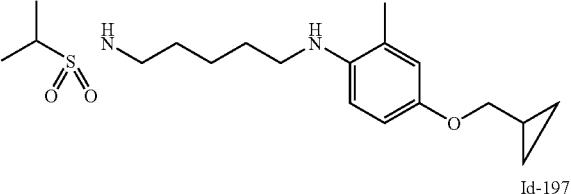
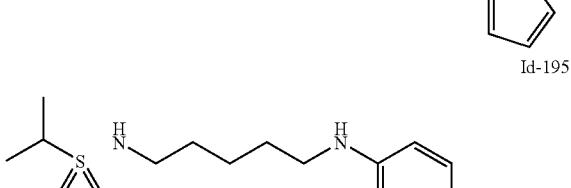
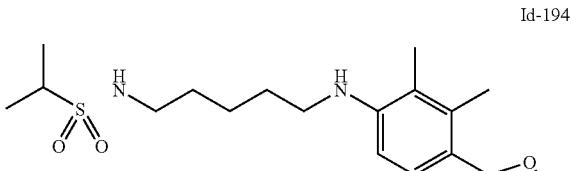
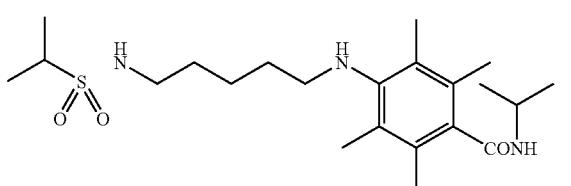
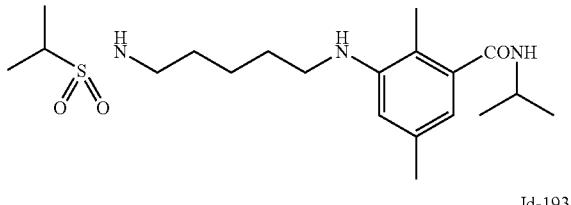
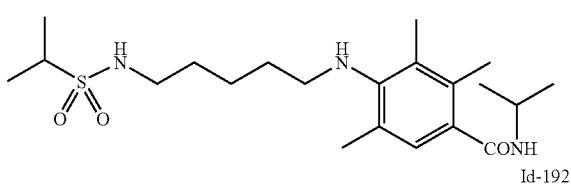
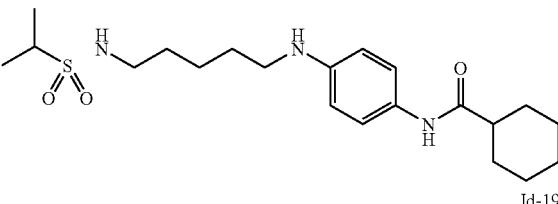
50 Id-188



55 Id-189

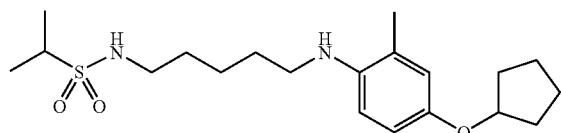
**276**
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Id-190



277
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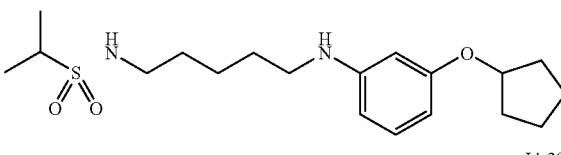
Id-198



[Formula 144]

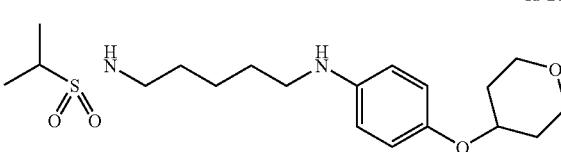
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Id-199



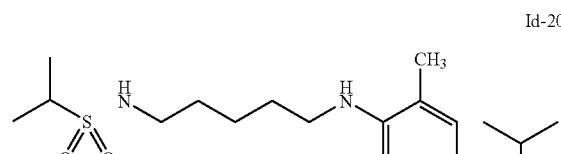
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Id-200



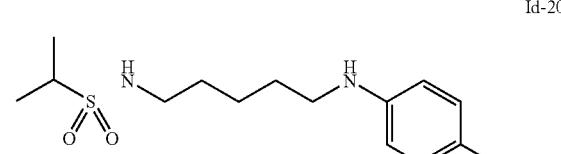
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Id-201



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Id-202



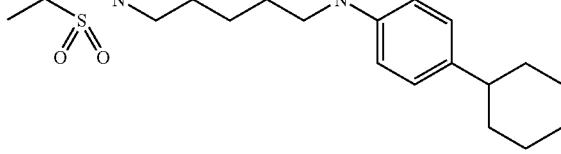
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Id-203



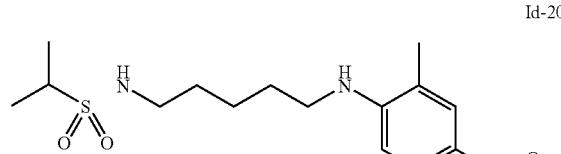
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Id-204



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Id-205



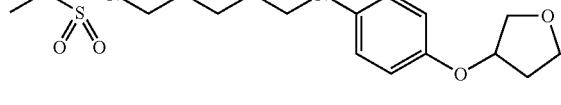
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Id-206



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Id-207

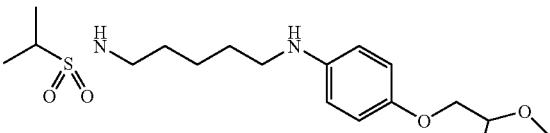


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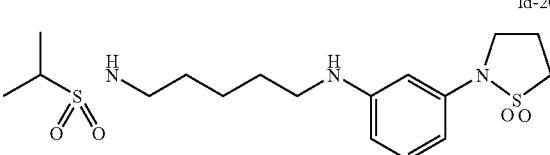
Id-208

278
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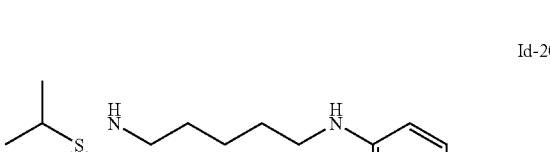
Id-206



Id-199



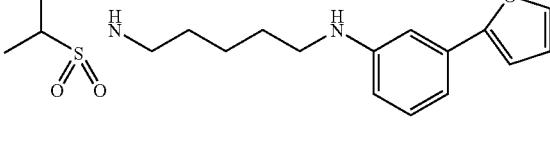
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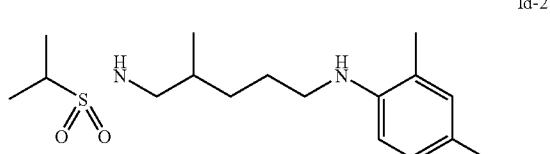
Id-201



Id-202



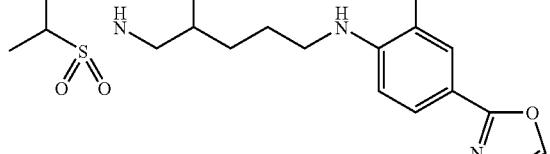
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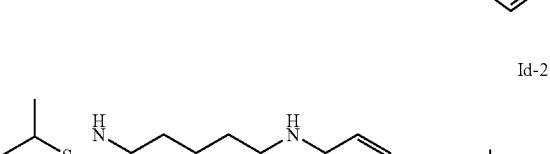
Id-204



Id-205



Id-206



Id-207

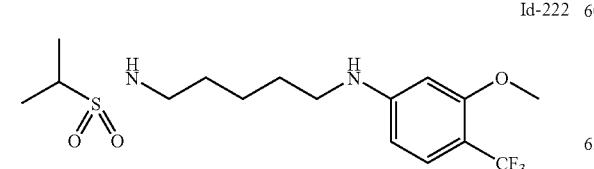
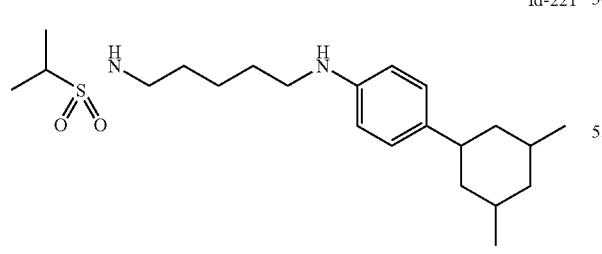
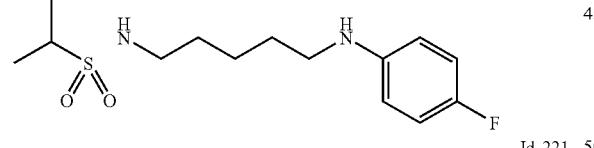
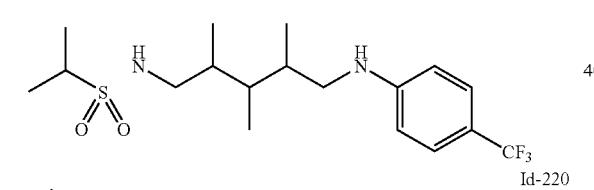
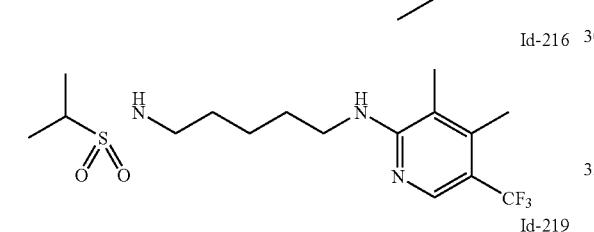
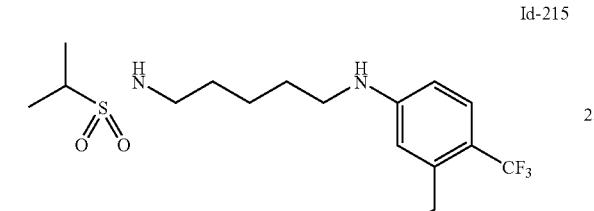
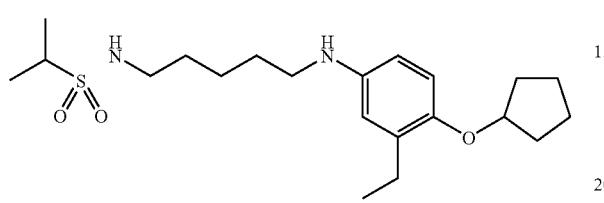
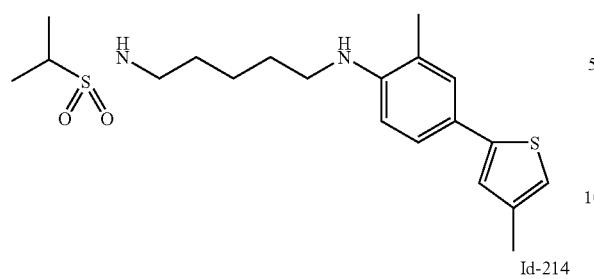


Id-208

279

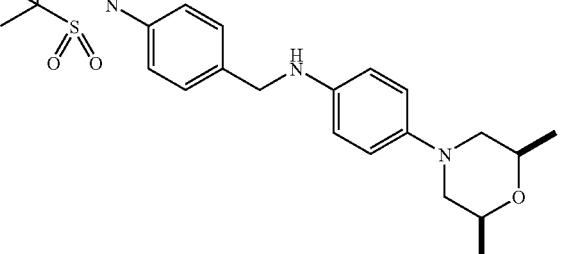
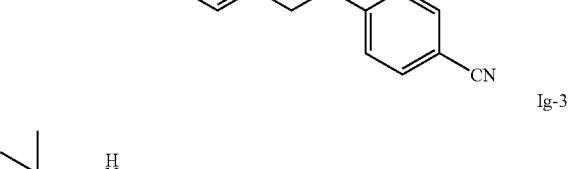
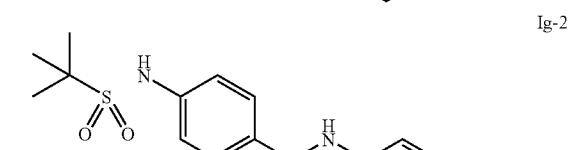
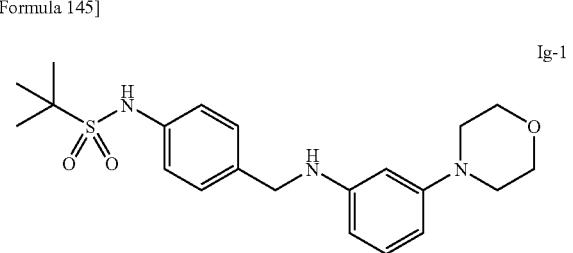
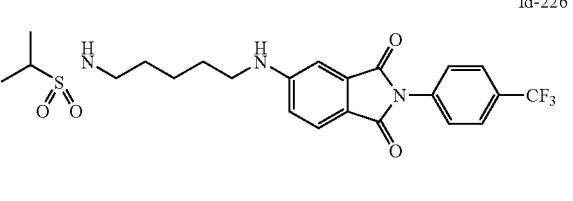
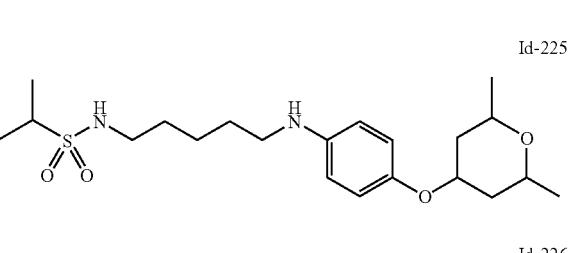
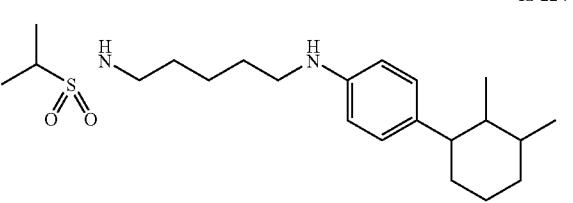
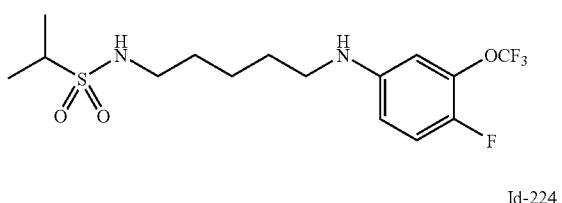
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Id-213

**280**

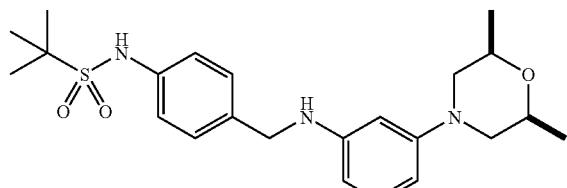
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Id-223

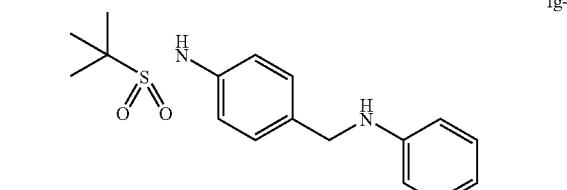


281

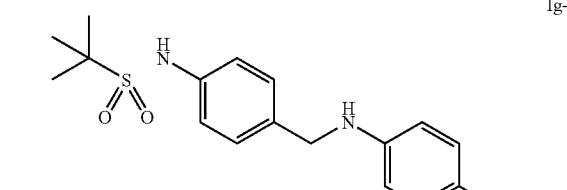
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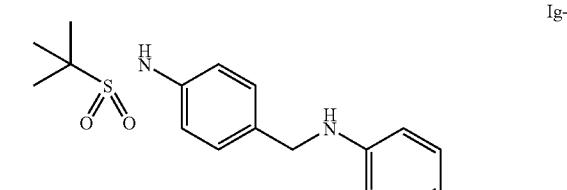
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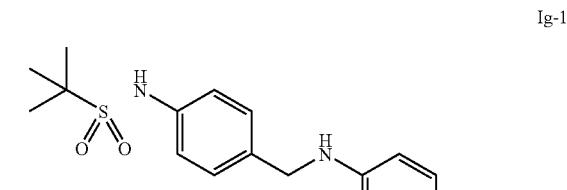
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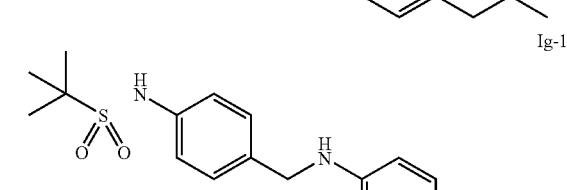
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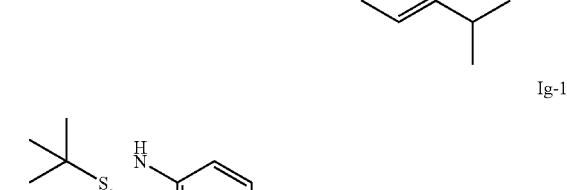
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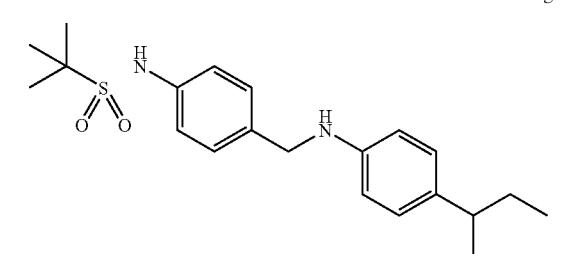
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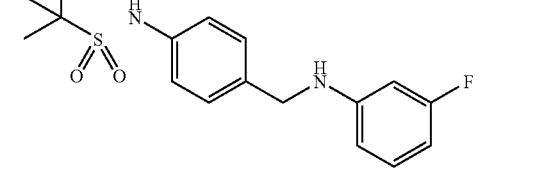
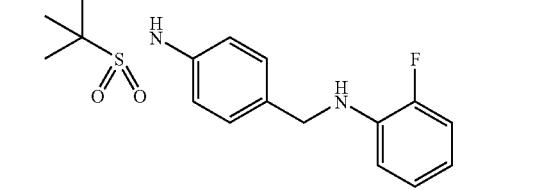
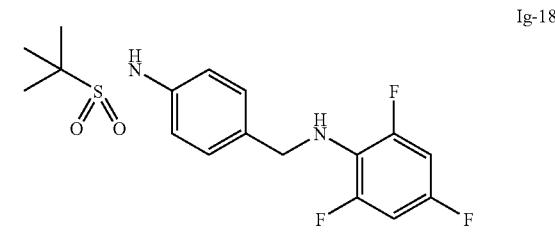
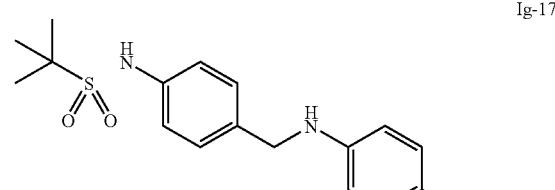
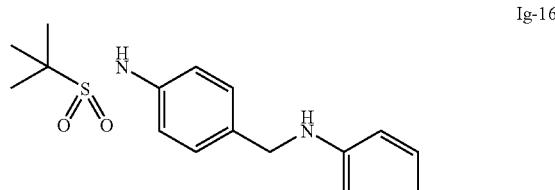
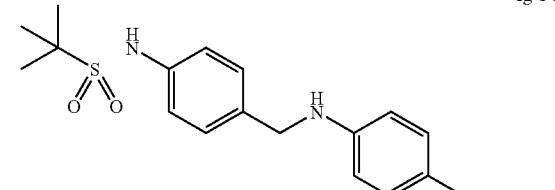
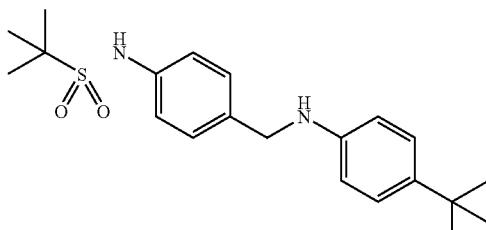
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60

65

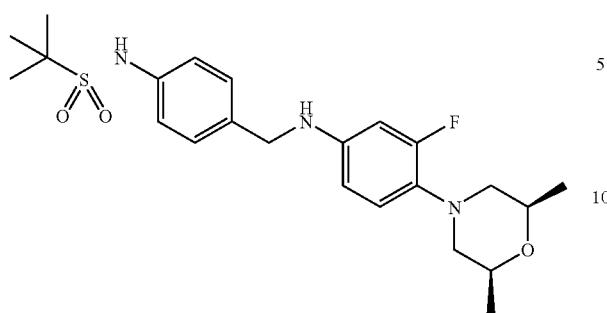
282

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283

-continued

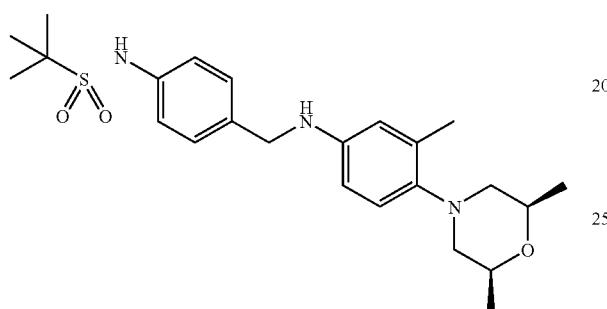


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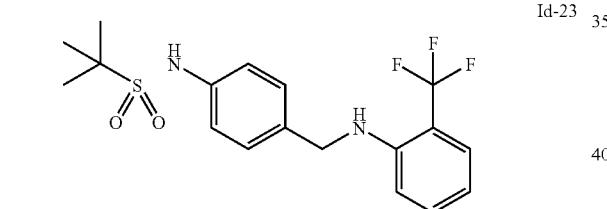
Ig-22



20

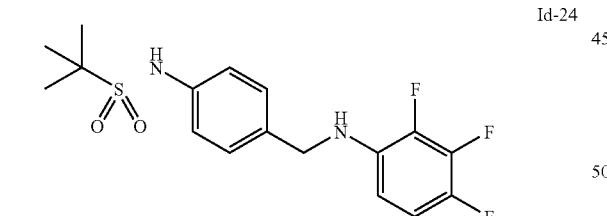
25

[Formula 146]



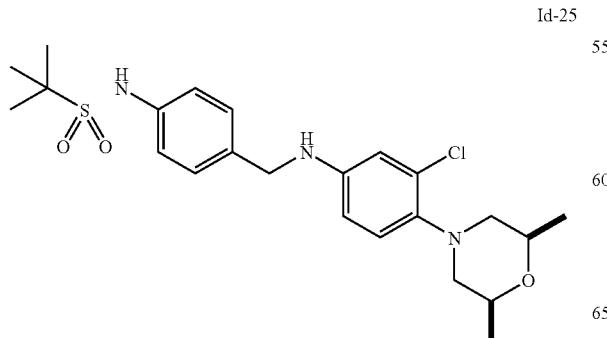
Id-23

Id-28



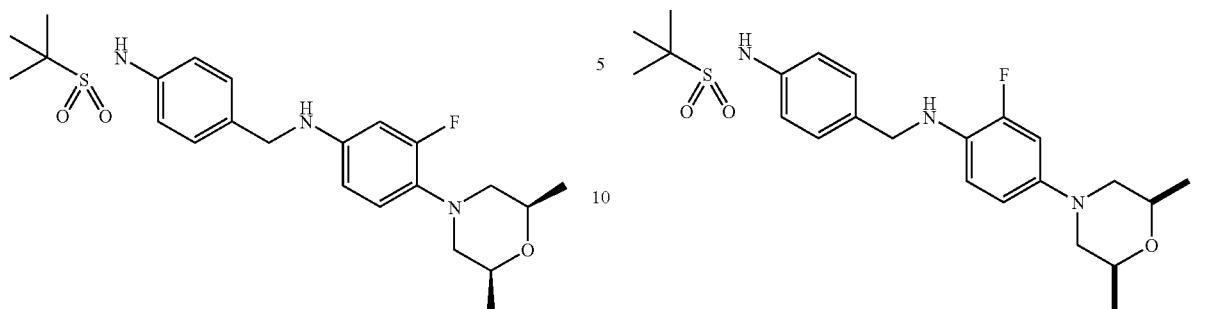
Id-24

Id-29



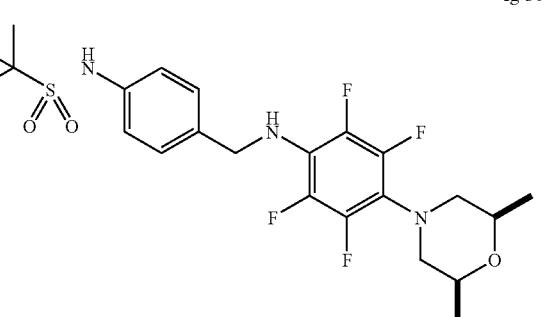
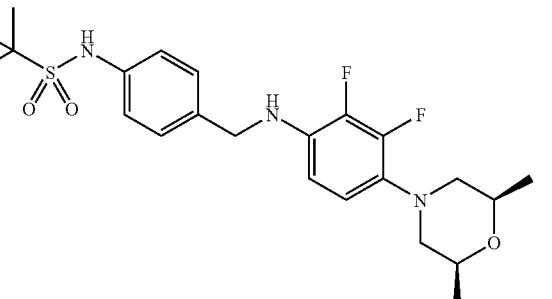
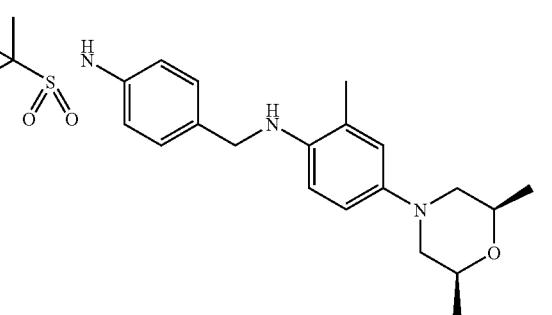
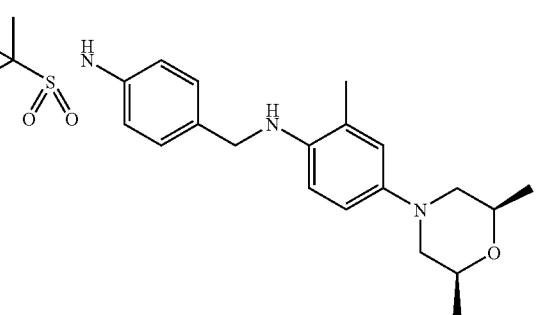
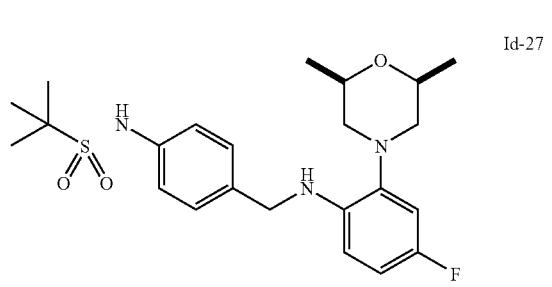
Id-25

Id-30

**284**

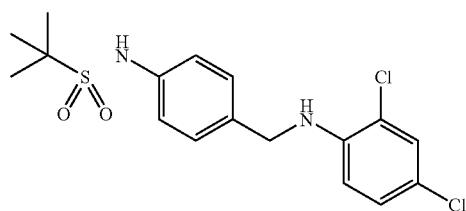
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Id-26

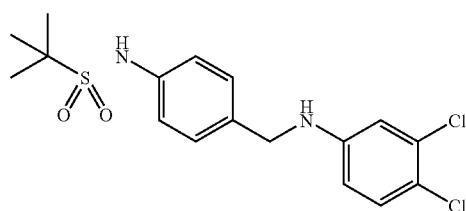


285

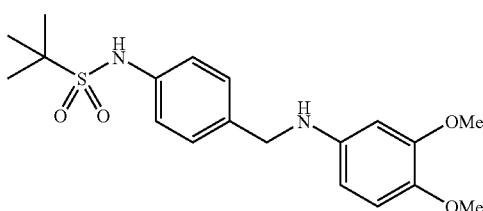
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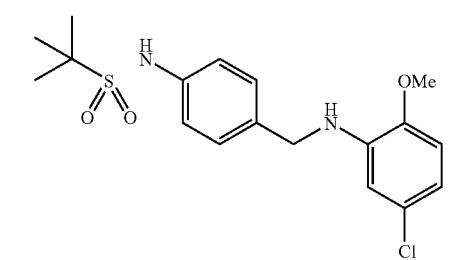
Ig-31



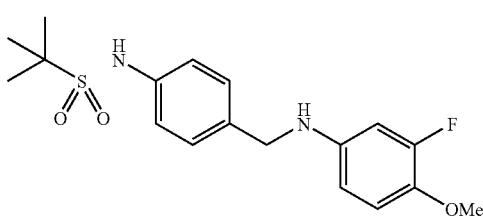
Ig-32



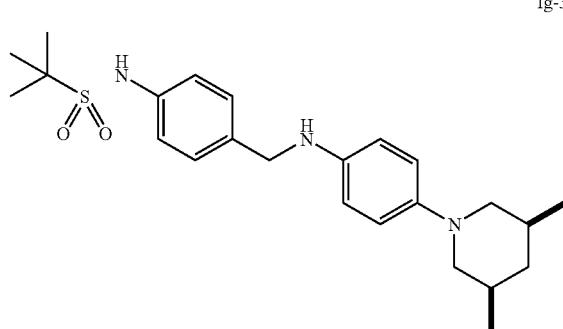
Ig-33



Ig-35



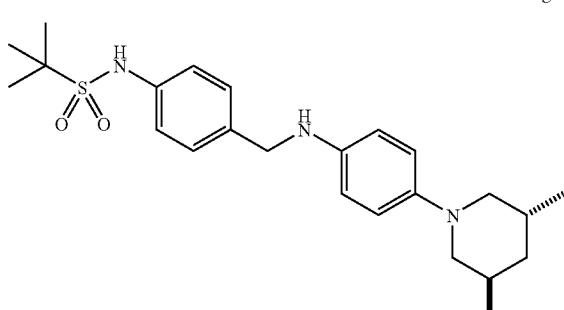
Ig-36



Ig-37

286

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Ig-38

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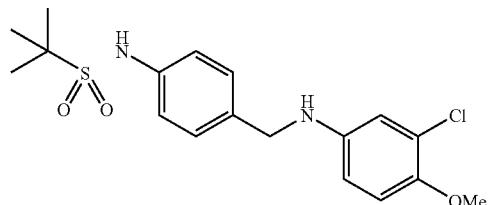
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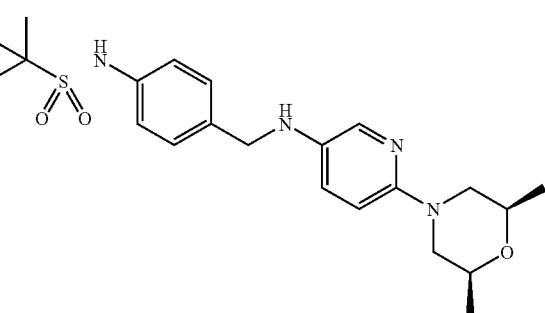
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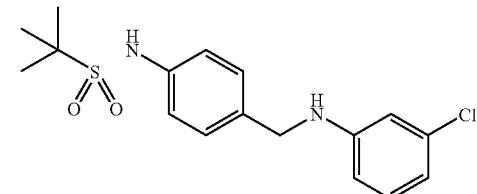
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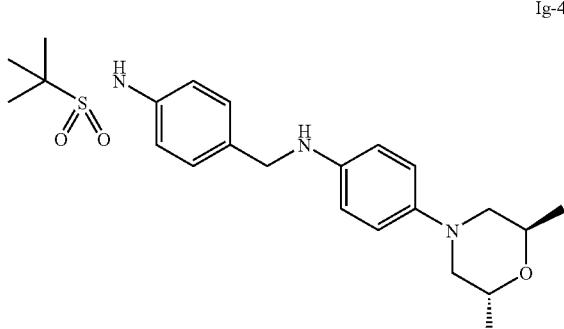
Ig-39



Ig-40



Ig-41

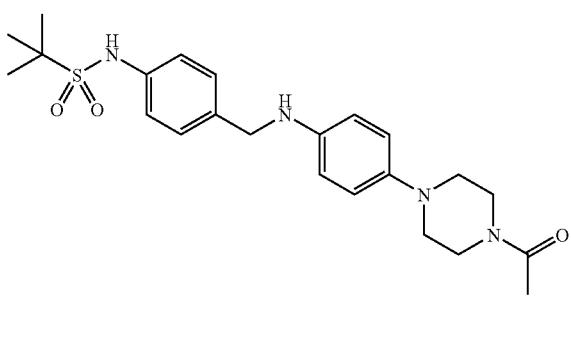


Ig-42

287

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Ig-43



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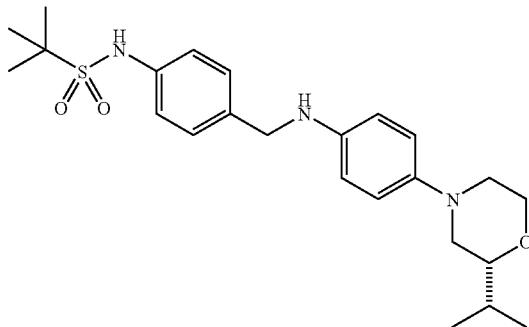
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288

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Ig-47



Ig-44

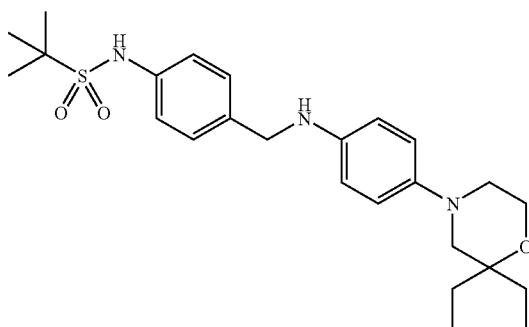
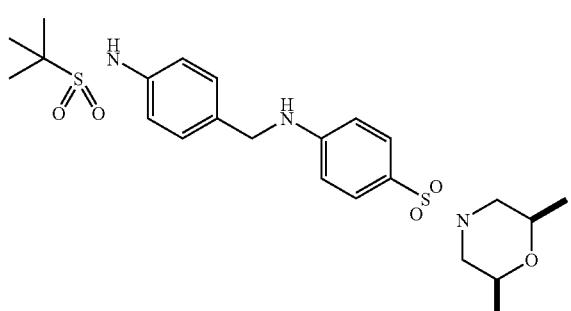
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Ig-48



[Formula 147]

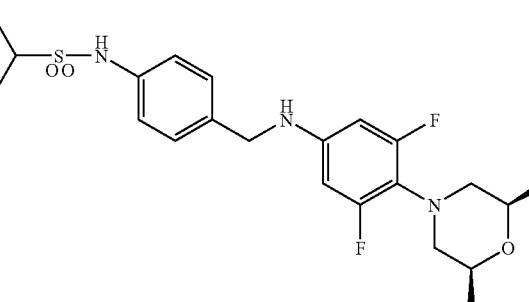
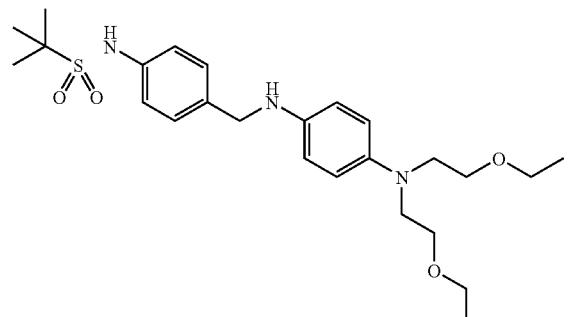
Ig-45

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Ig-49

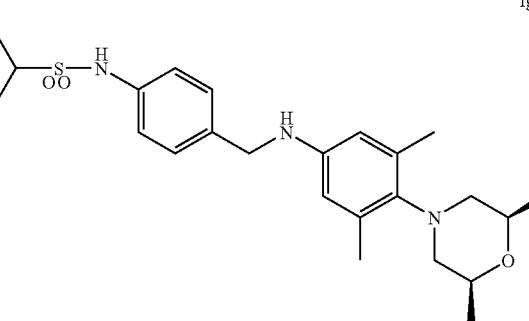
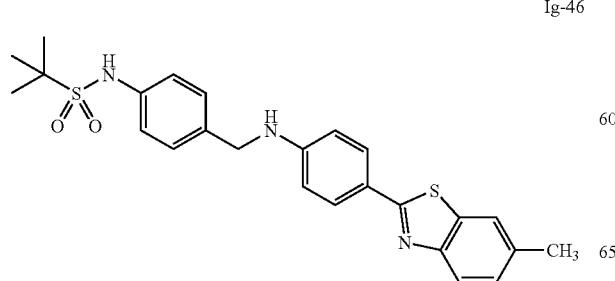


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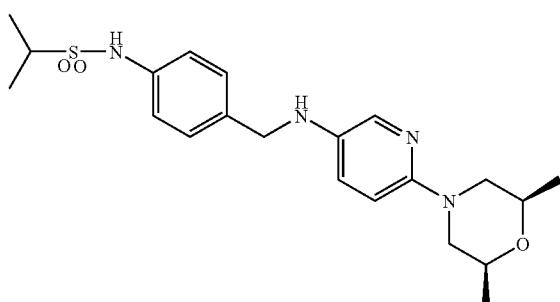
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Ig-50



289

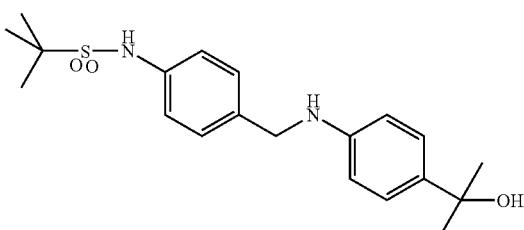
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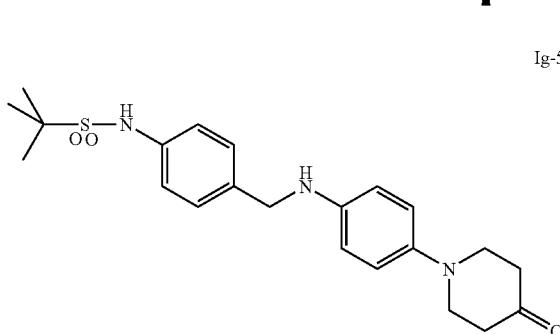
Ig-51

290

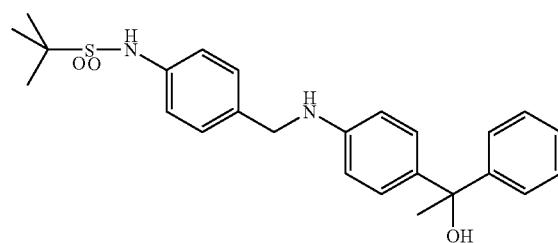
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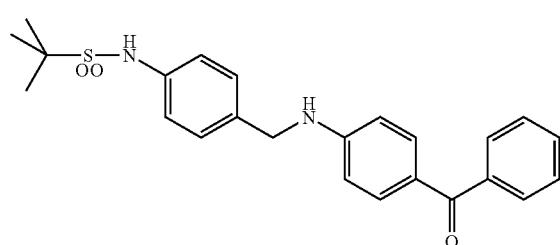
Ig-56



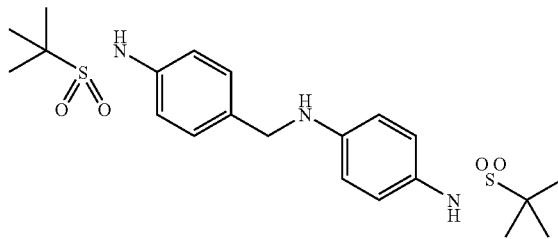
Jg-52



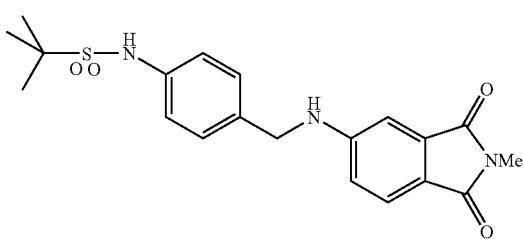
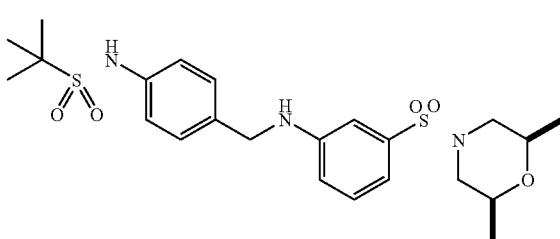
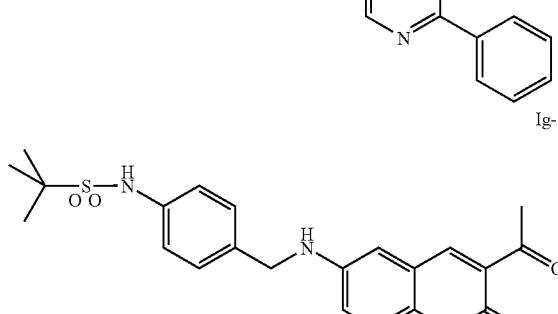
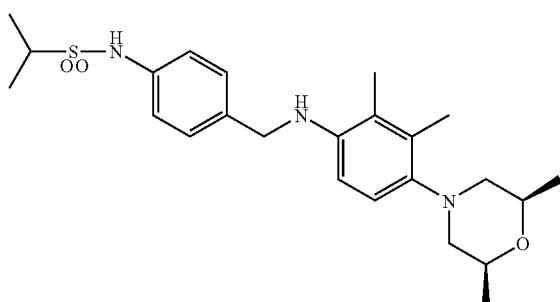
Ig-58



Ig-53

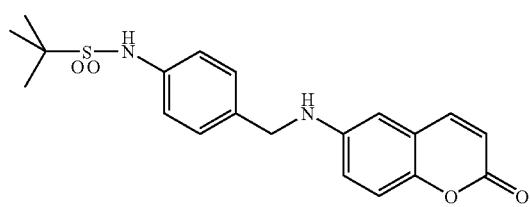


Ig-59

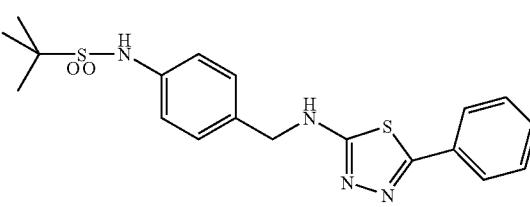
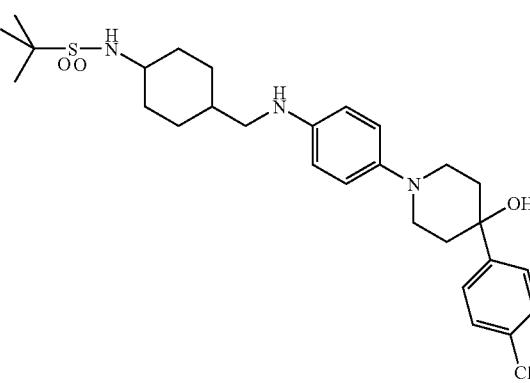
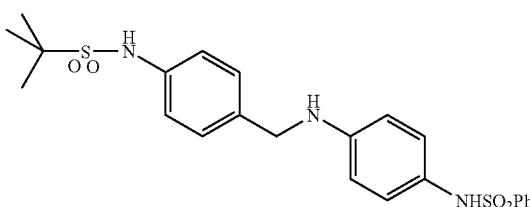
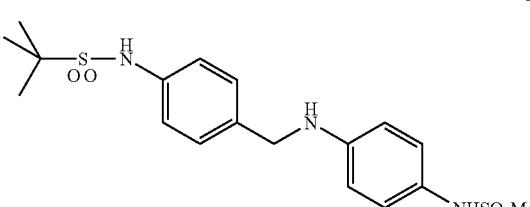


291

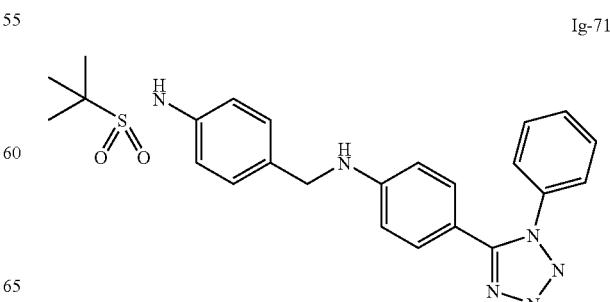
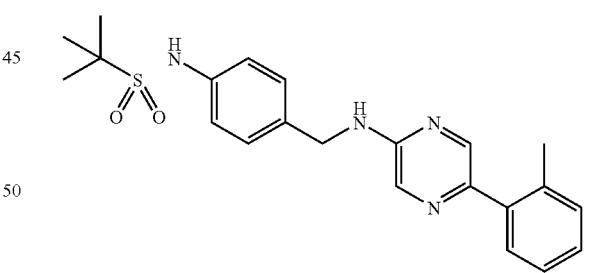
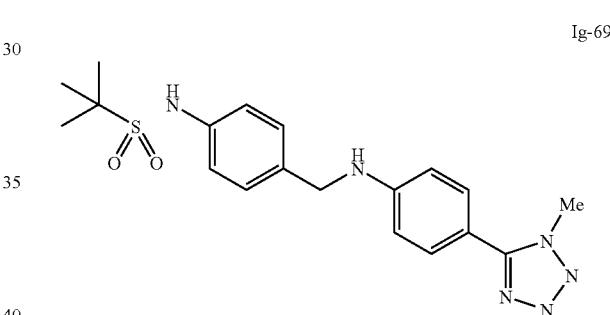
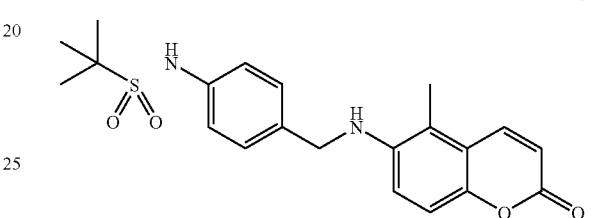
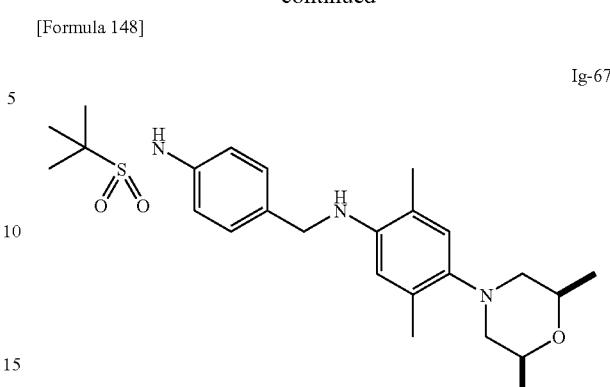
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[Formula 148]

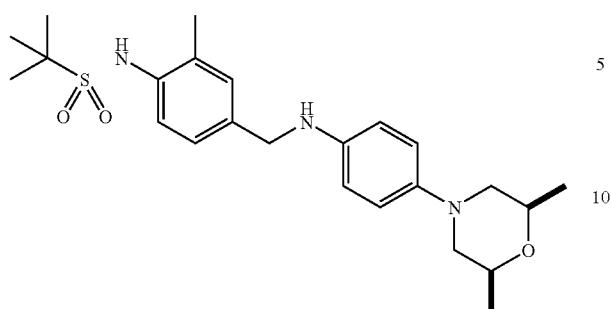
**292**

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293

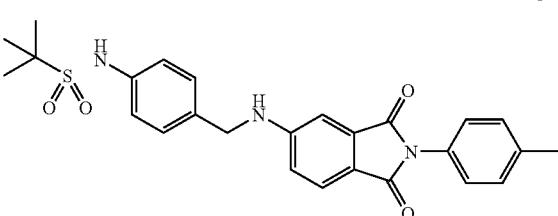
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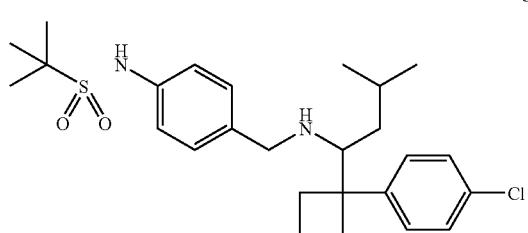
Ig-74

294

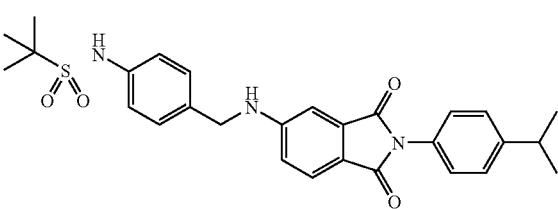
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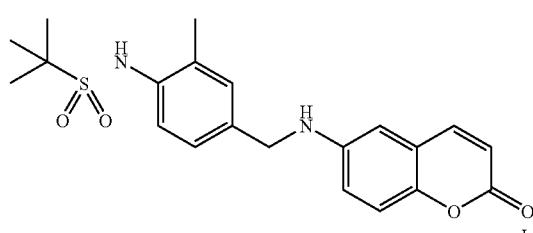
Ig-80



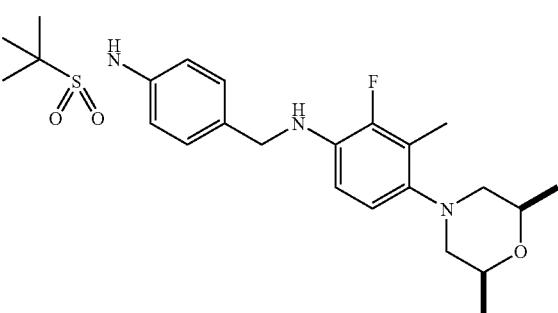
Ig-75



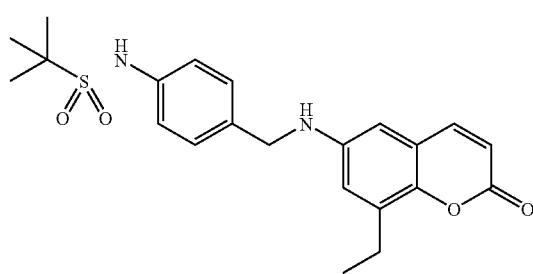
Ig-82



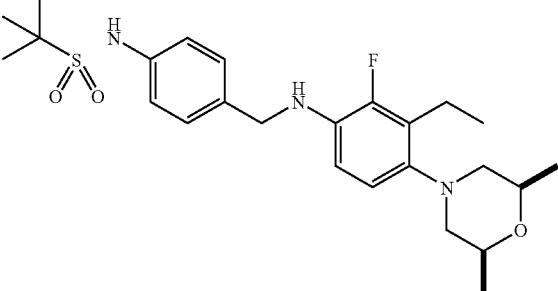
Ig-76



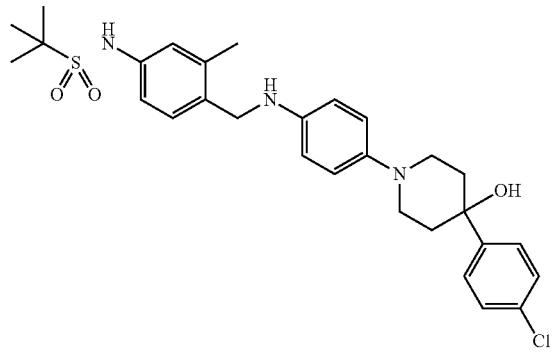
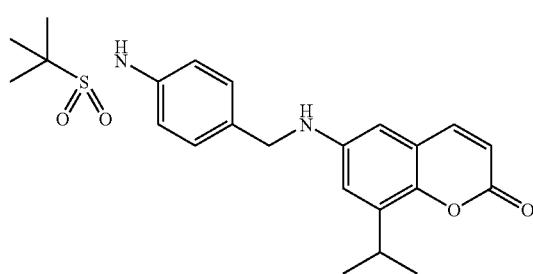
Jg-83



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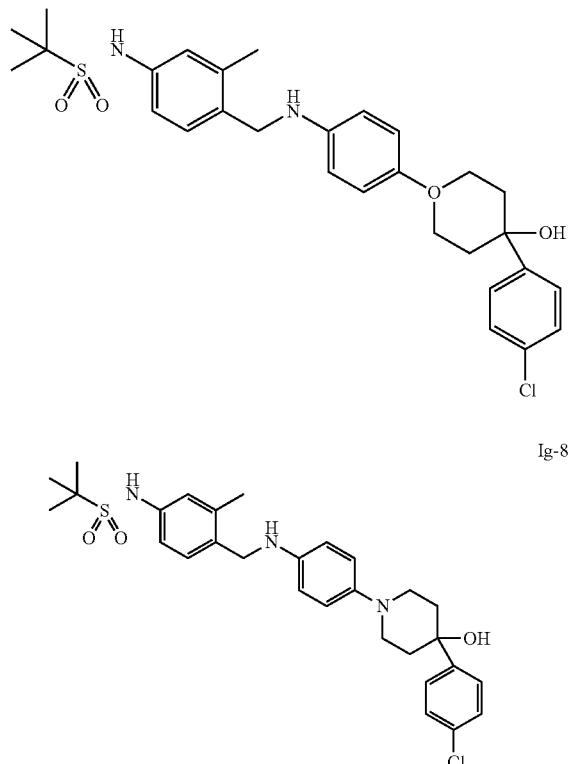


JG-84



295

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Ig-85

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Ig-86 20

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Ig-87 35

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Ig-88 45

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Ig-89

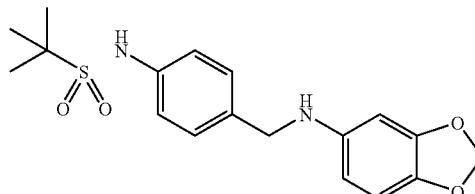
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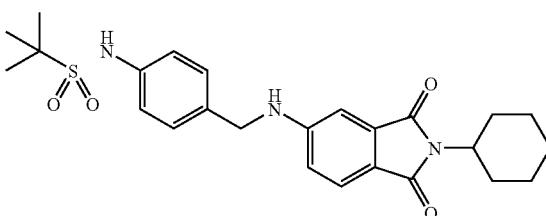
296

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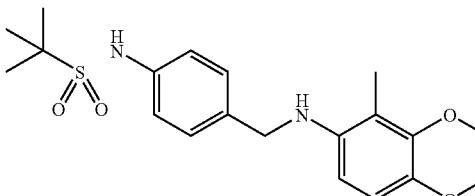
Ig-90



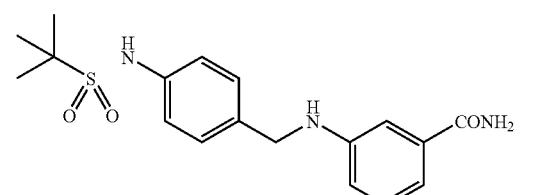
Ig-91



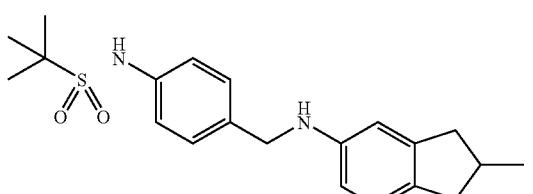
Ig-92



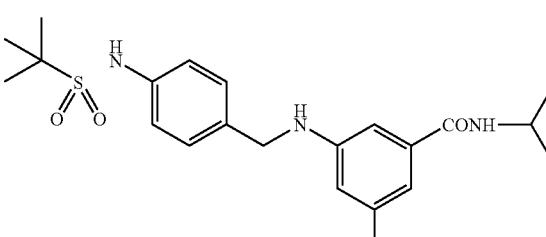
Ig-93



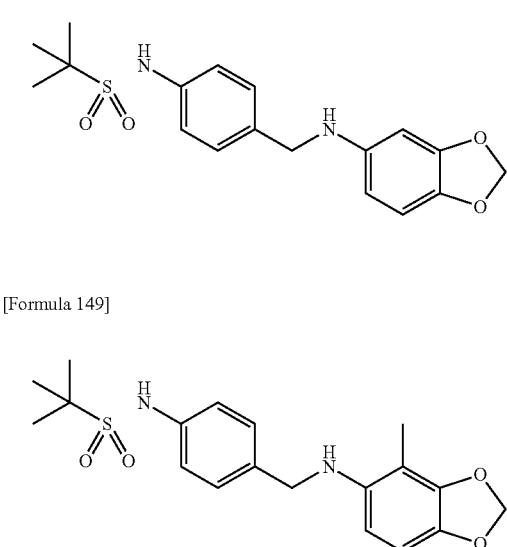
Ig-94



Ig-95



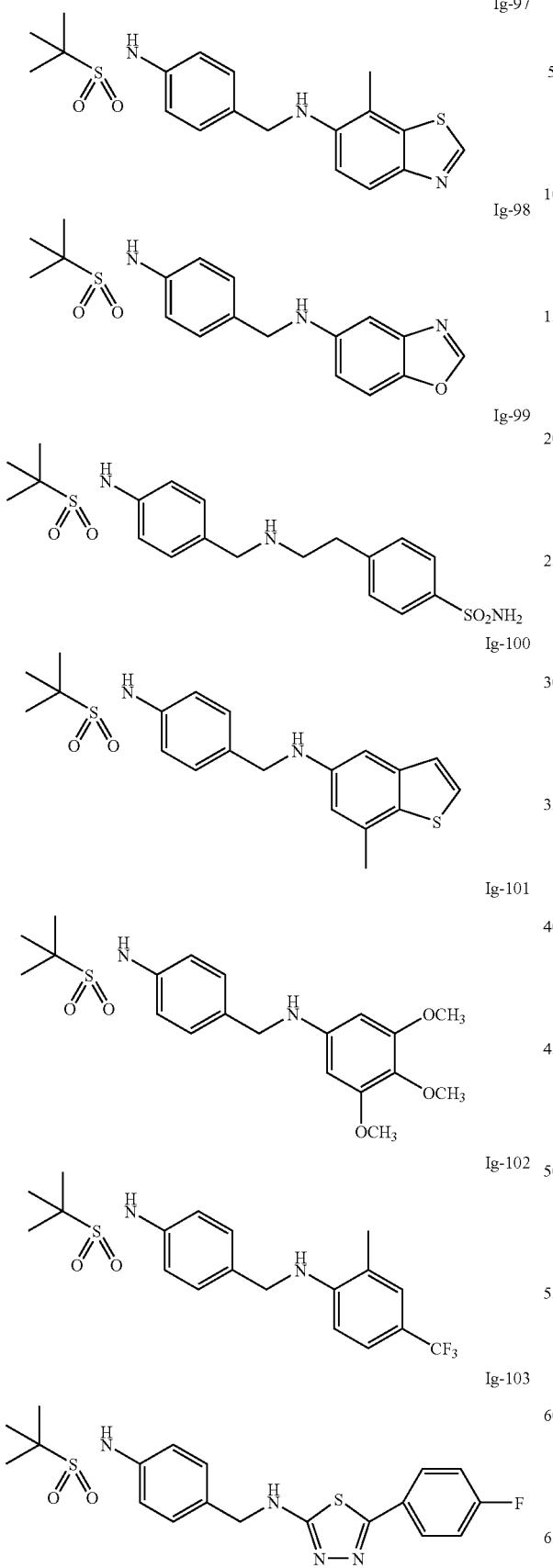
Ig-96



[Formula 149]

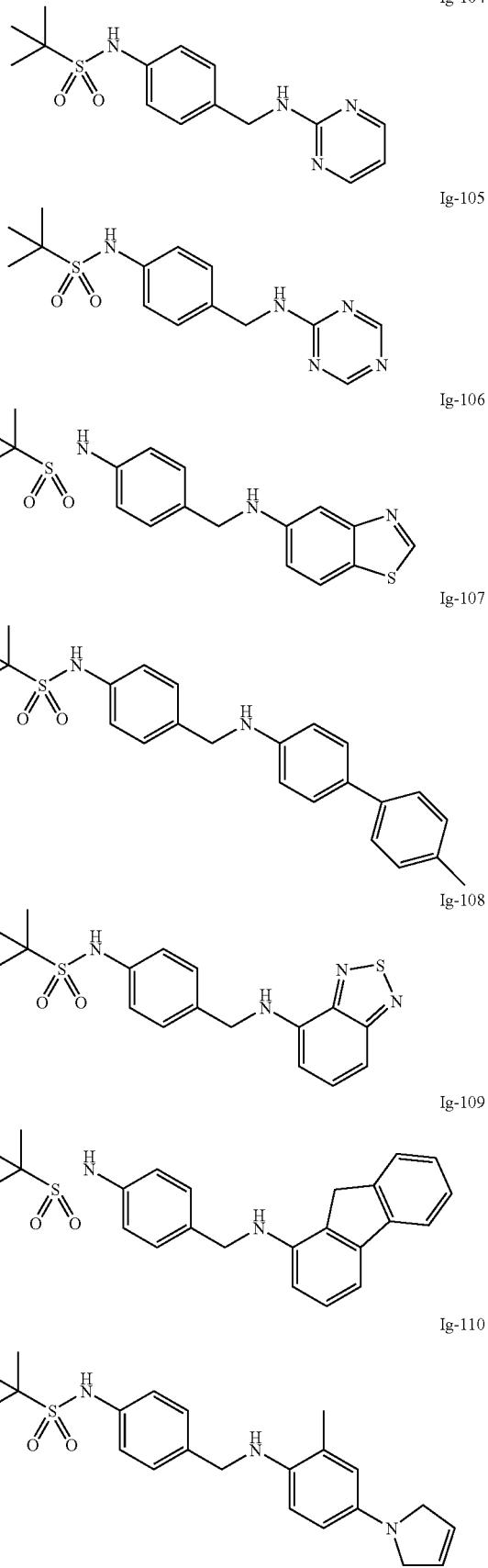
297

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**298**

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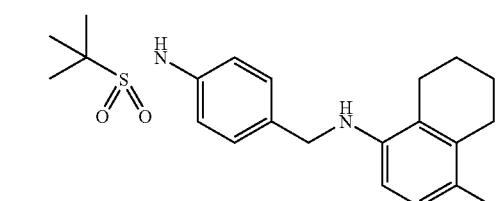
Ig-104



299

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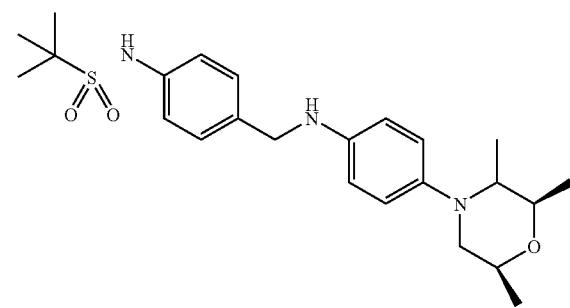
[Formula 150]



Ig-111

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Ig-112



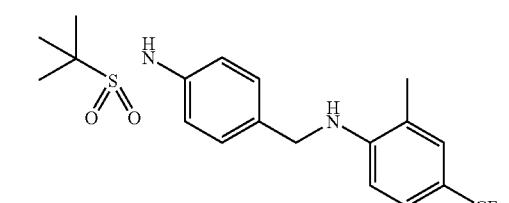
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Ig-113

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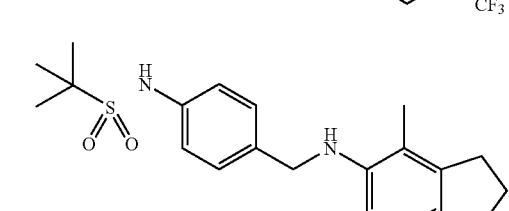


Ig-114

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Ig-115

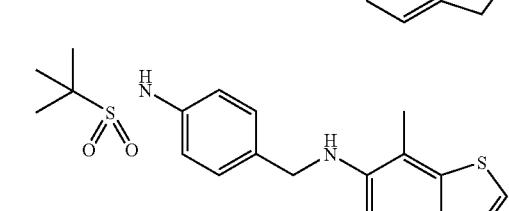
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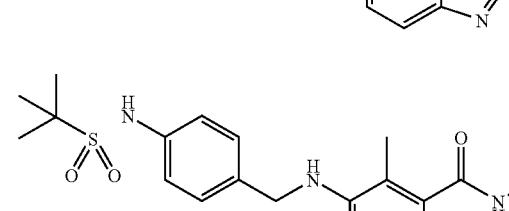
Ig-116

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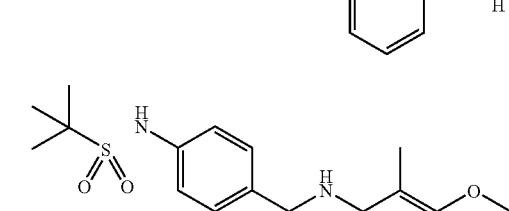
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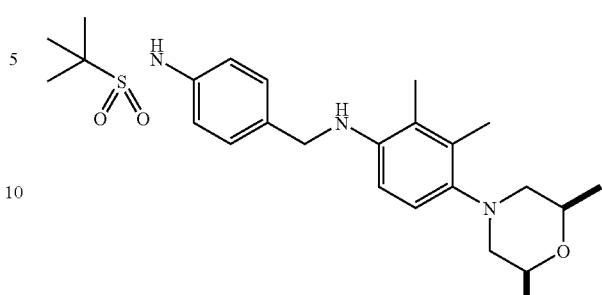
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Ig-118



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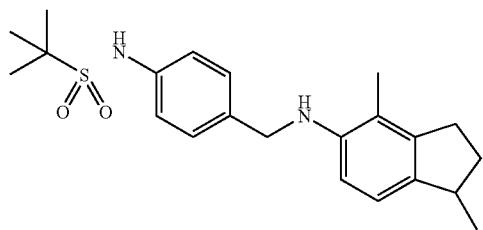
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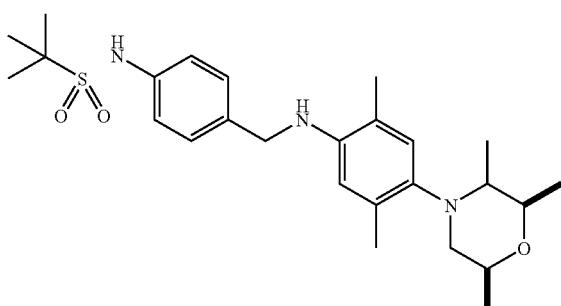
301

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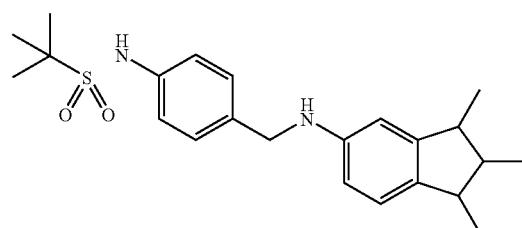
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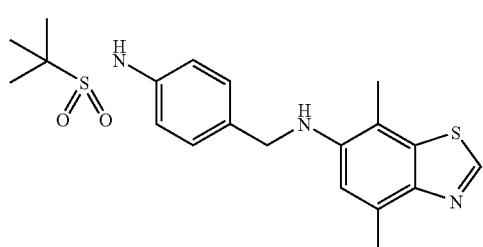
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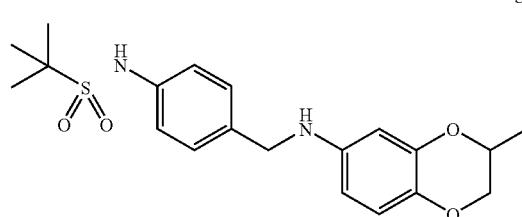
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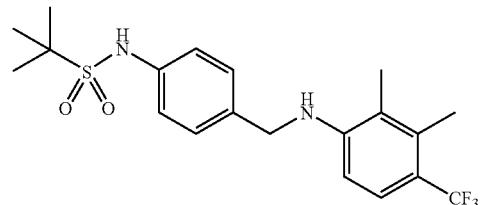
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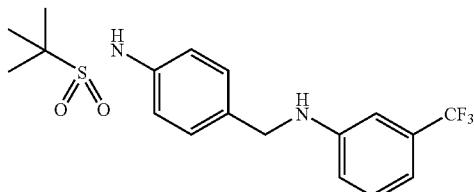


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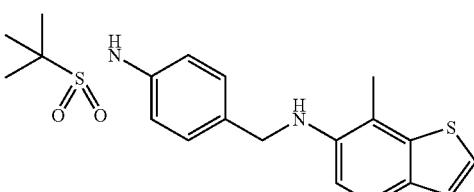
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302

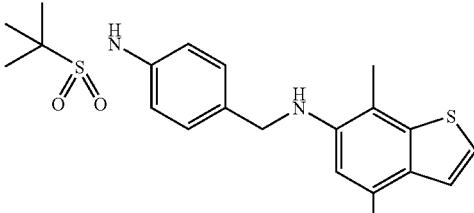
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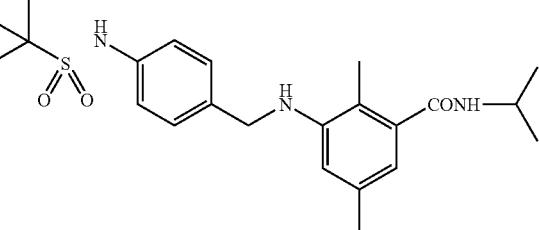
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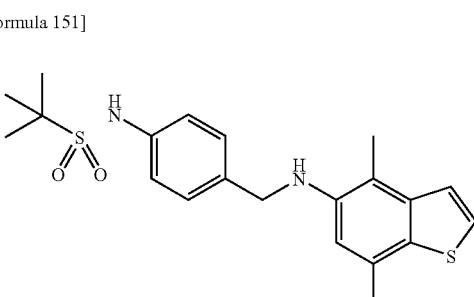
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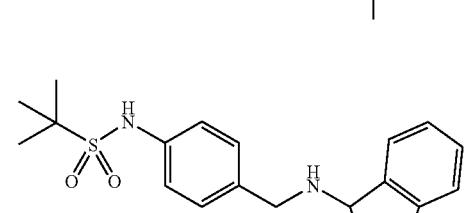
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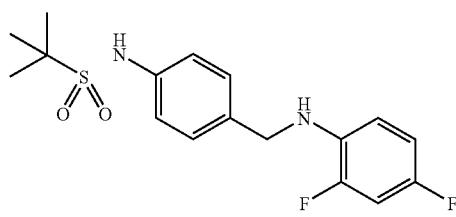
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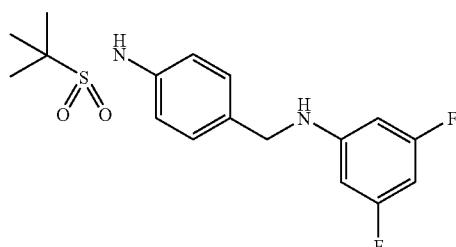
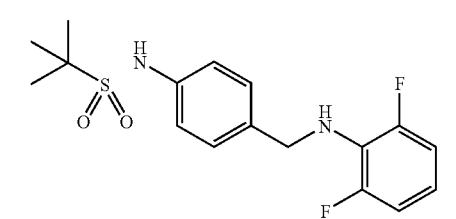
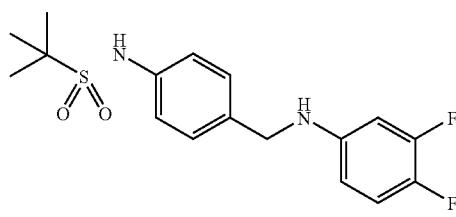
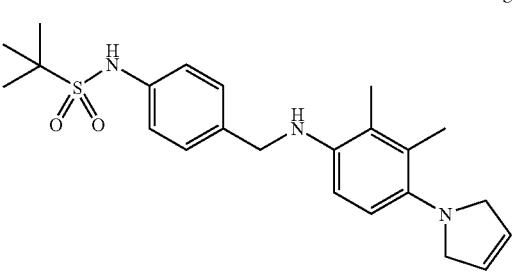
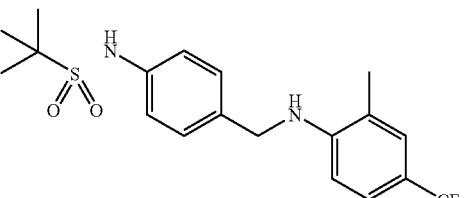
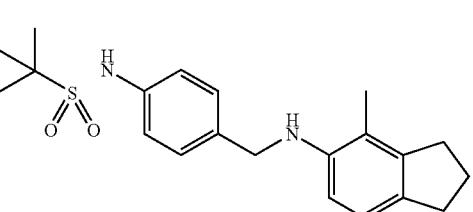
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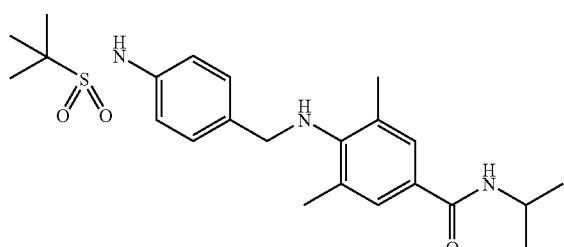
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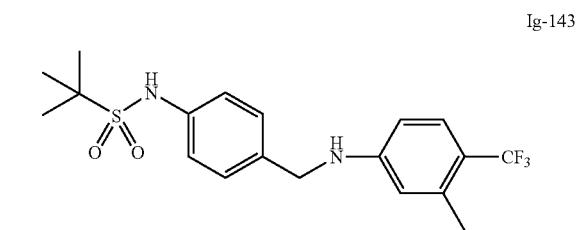
Ig-135

Ig-136
10Ig-137
15Ig-138
20Ig-139
25Ig-140
30Ig-141
35**304**

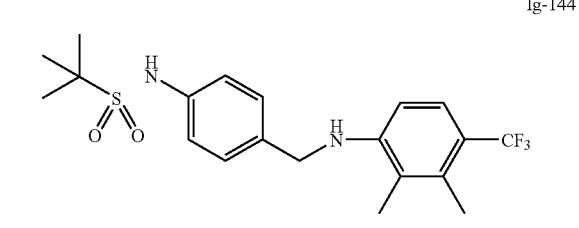
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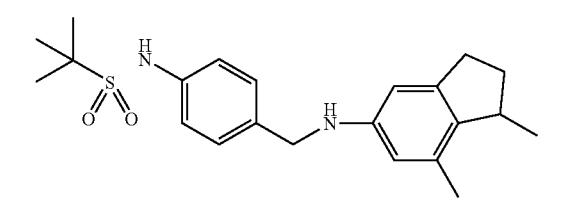
Ig-142



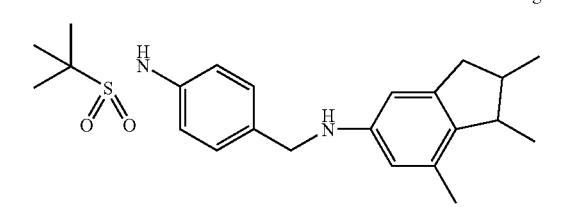
Ig-143



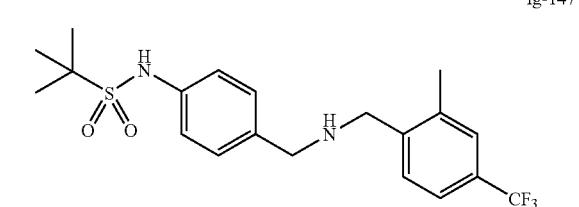
Ig-144



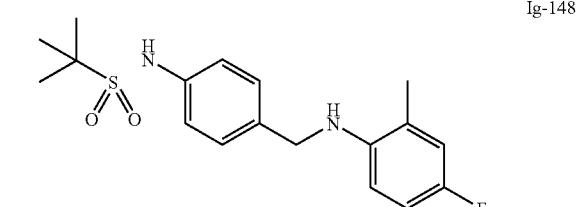
Ig-145



Ig-146



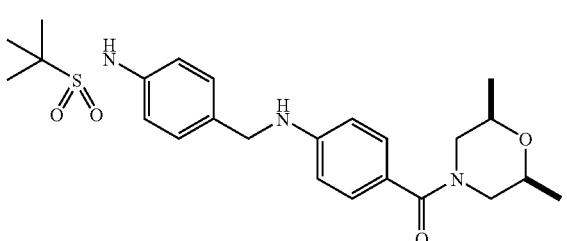
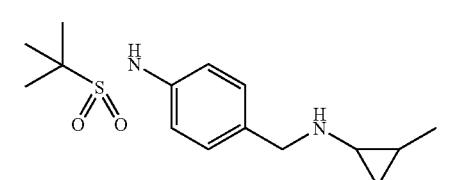
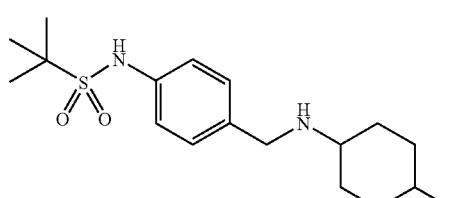
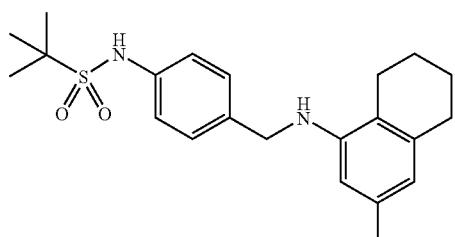
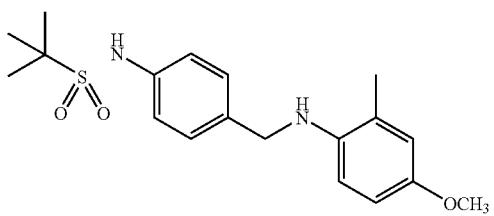
Ig-147



Ig-148

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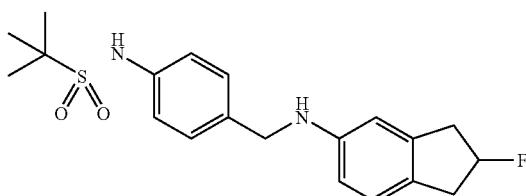
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[Formula 152]

306**306**

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Ig-149



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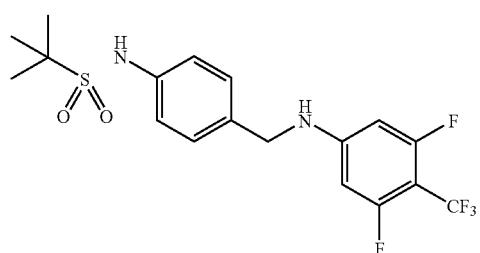
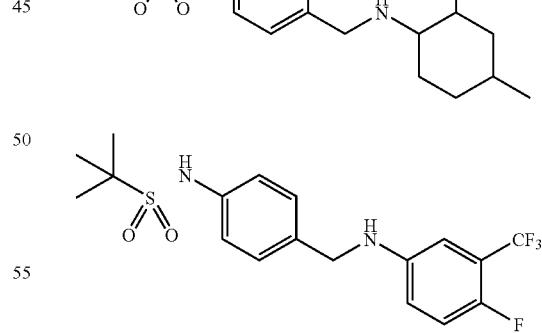
Ig-157

Ig-158

Ig-159

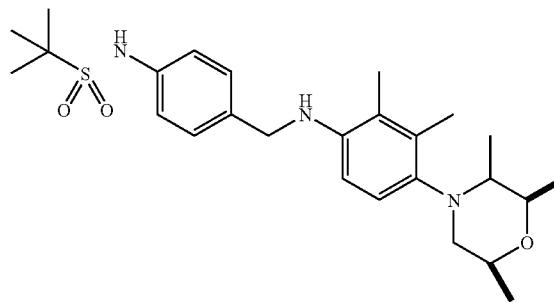
Ig-160

Ig-161

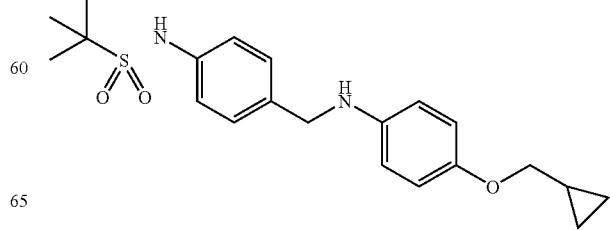
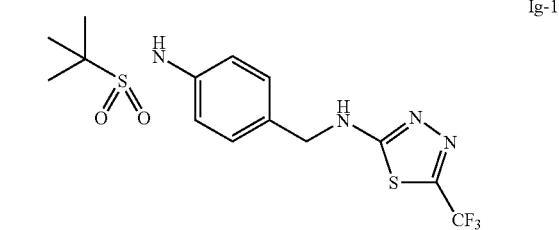
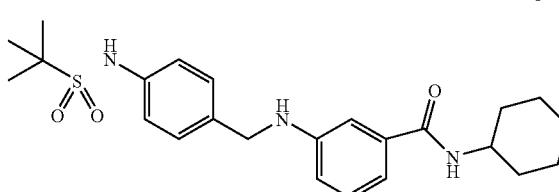
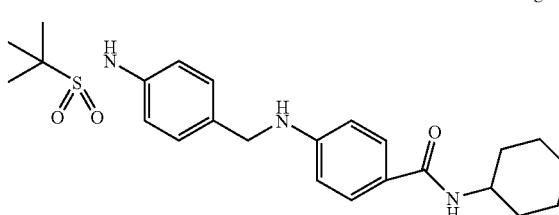
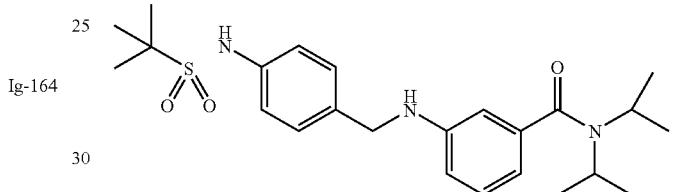
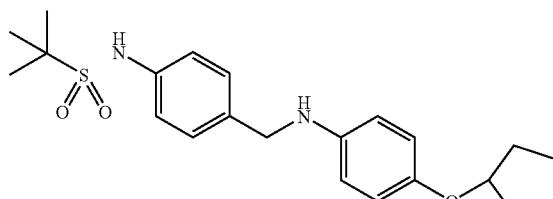
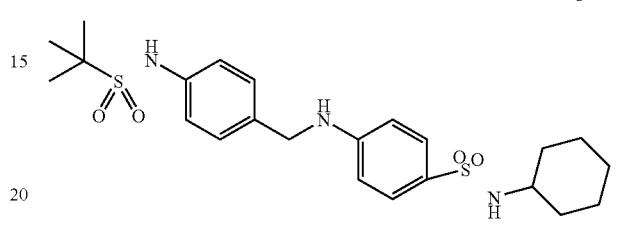
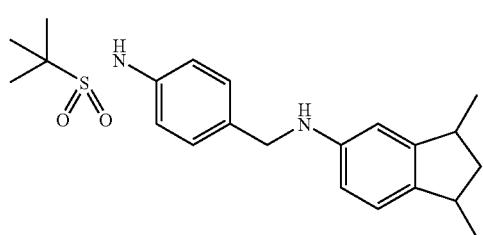
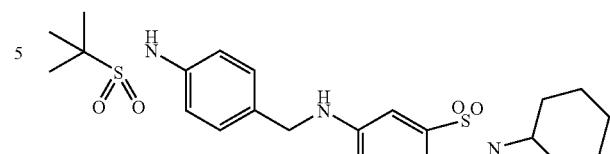


307

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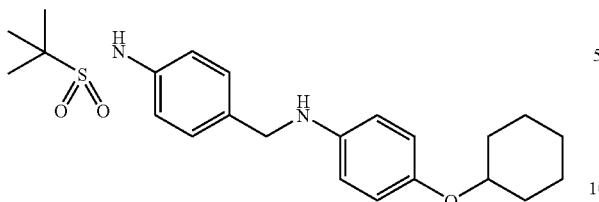
**308**

-continued

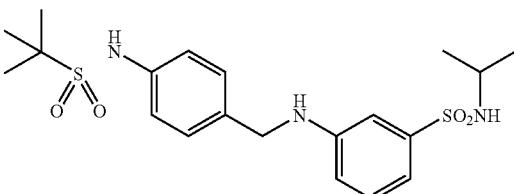


309

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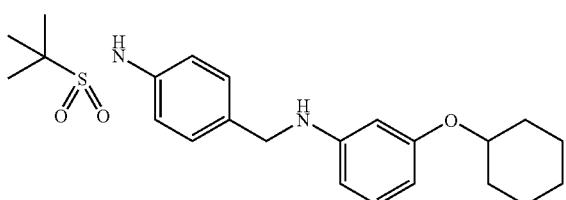


Ig-175

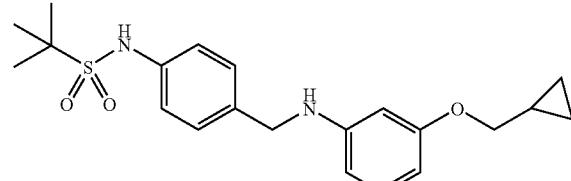


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Ig-181

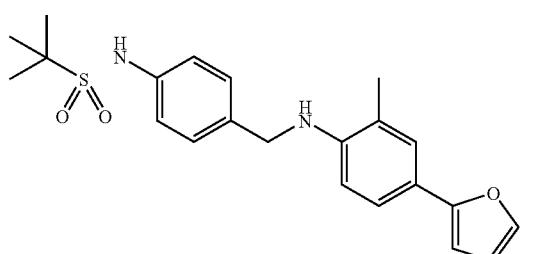


Ig-176

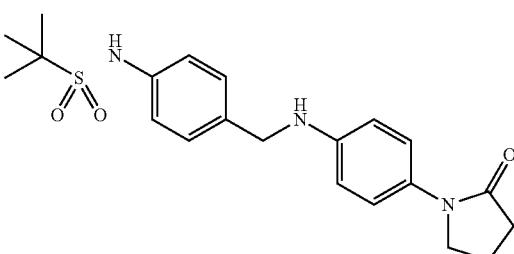


Ig-182

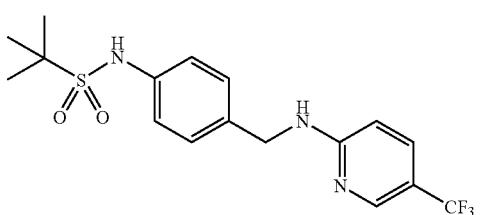
[Formula 153]



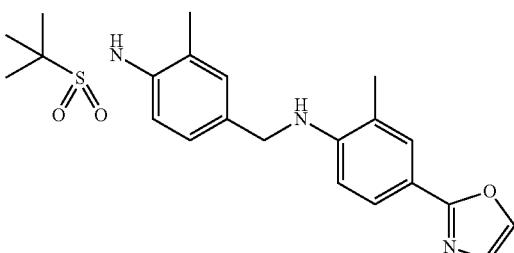
Ig-177 25



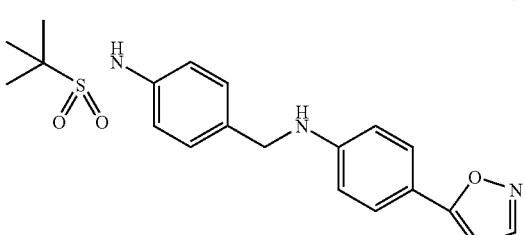
Ig-183



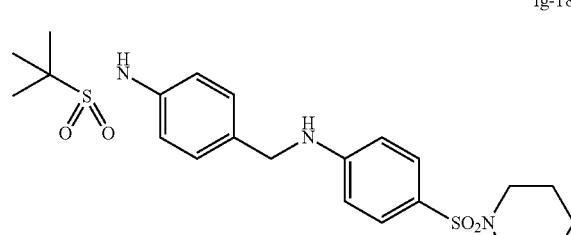
Ig-178



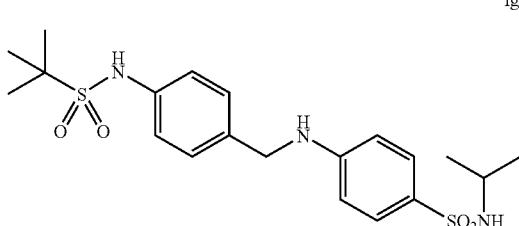
Ig-184



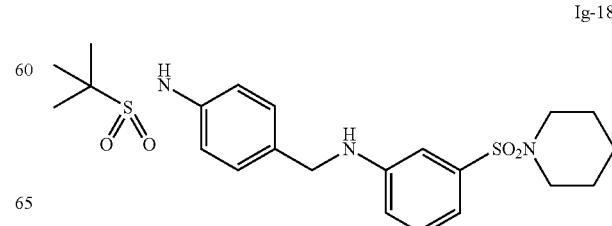
Ig-179



105



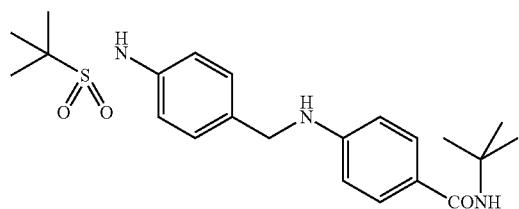
188



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311

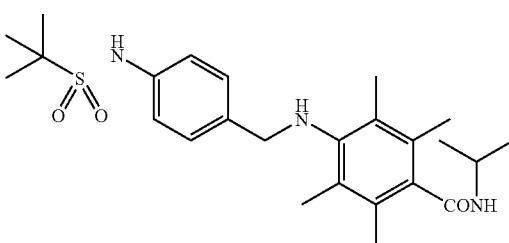
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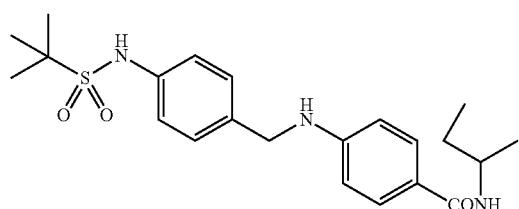
Ig-187

312

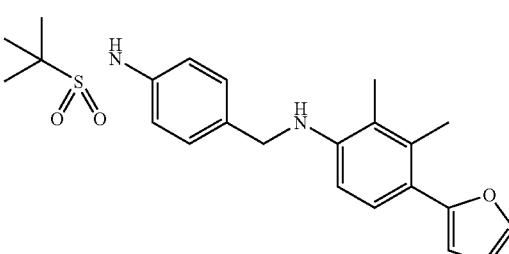
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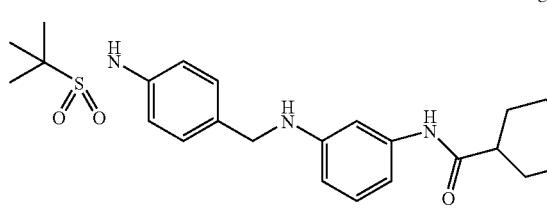
Ig-193



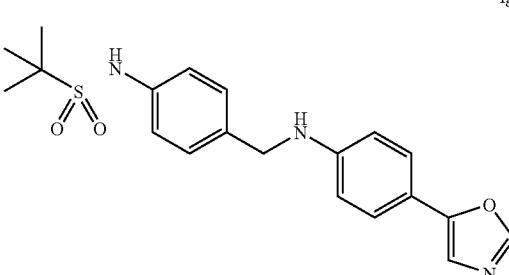
Ig-188



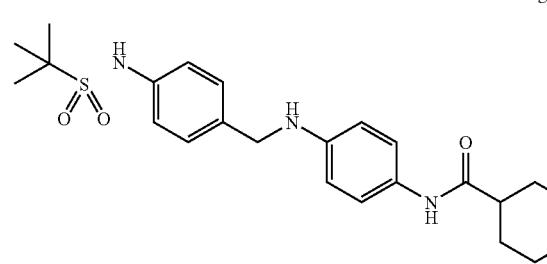
Ig-194



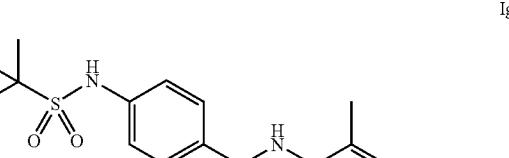
Ig-189



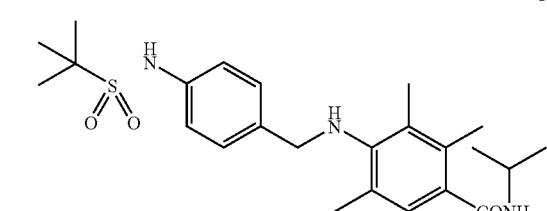
Ig-195



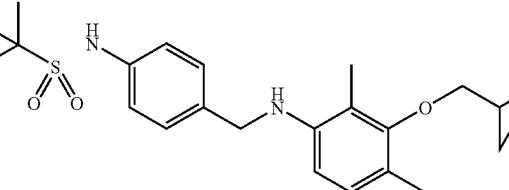
Ig-190



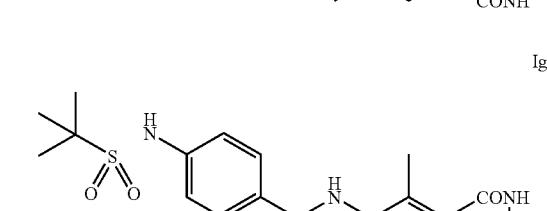
Ig-196



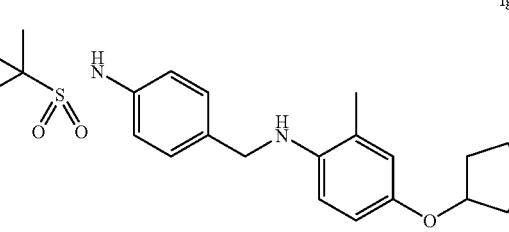
Ig-191



Ig-197



Ig-192

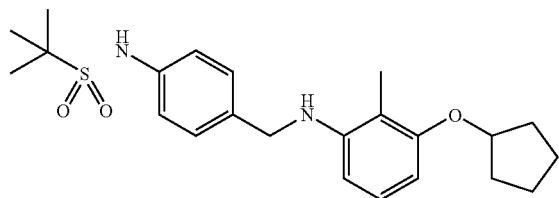


Ig-198

313

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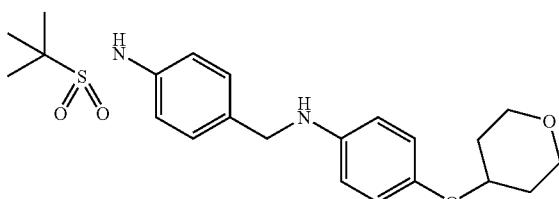
[Formula 154]



Ig-199

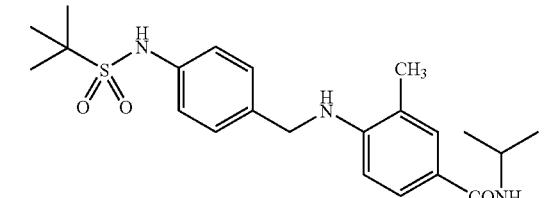
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Ig-200



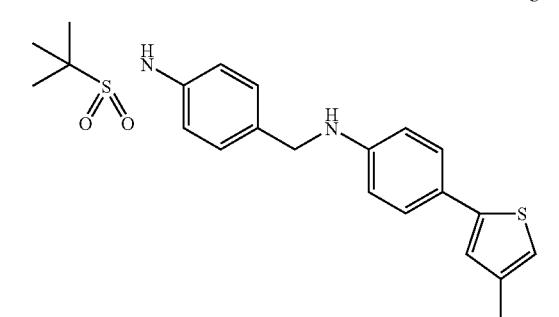
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Ig-201



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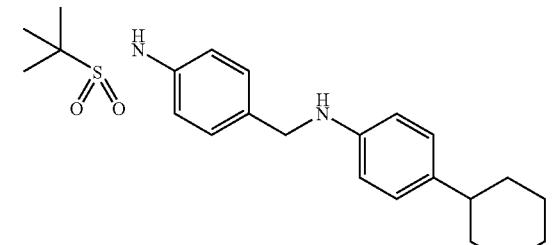
Ig-202



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Ig-203

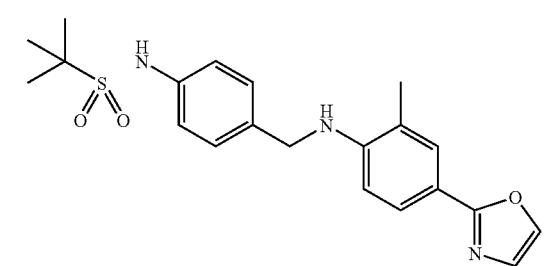
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Ig-204

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Ig-205

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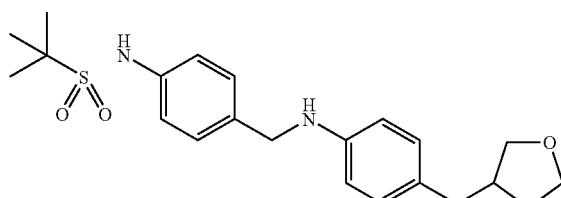


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314

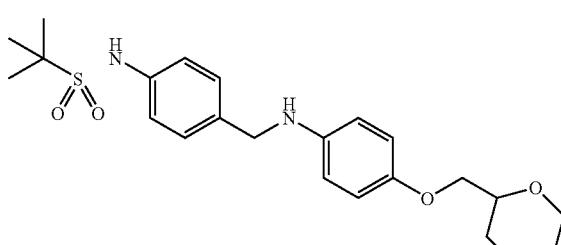
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Ig-205

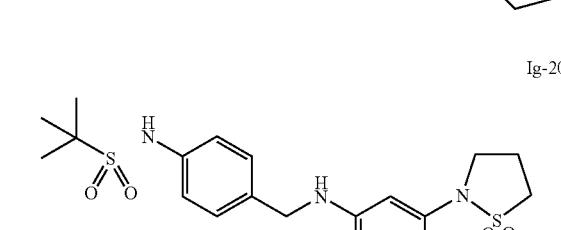


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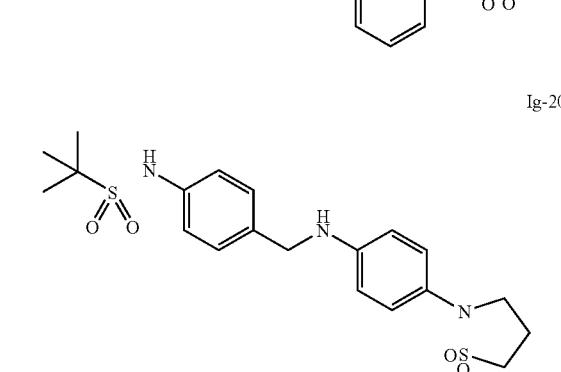
Ig-206



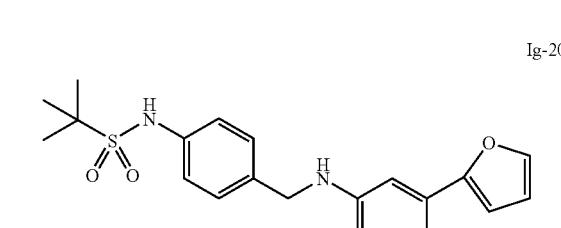
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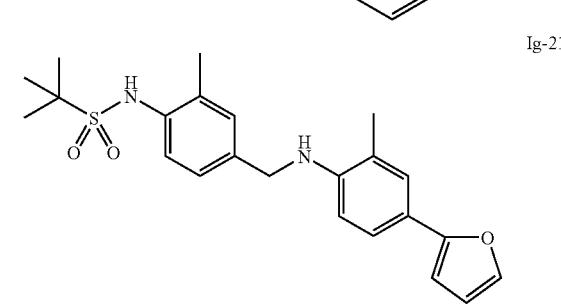
Ig-207



Ig-208



Ig-209

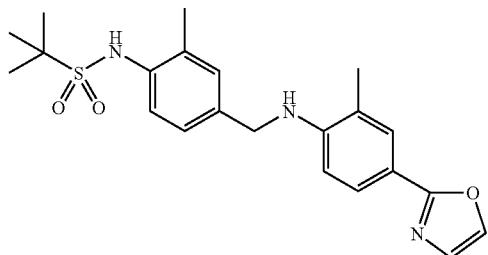


Ig-210

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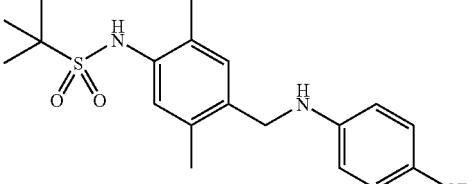
315

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Ig-211

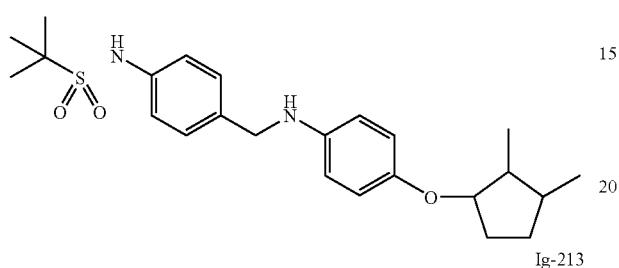
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**316**

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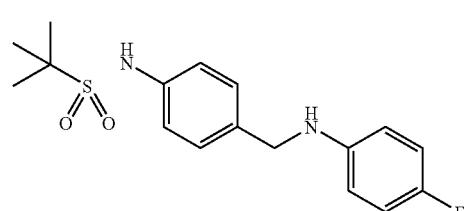
Ig-217

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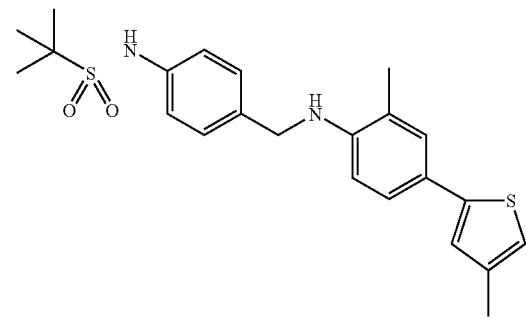
Ig-212

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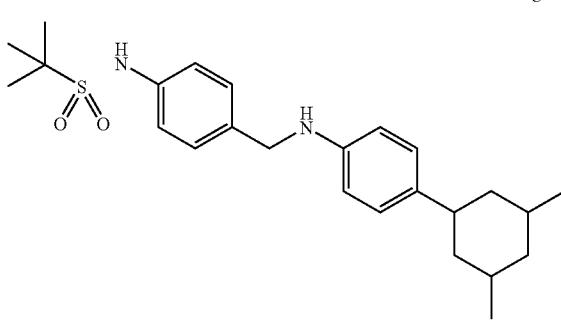
Ig-220

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Ig-213

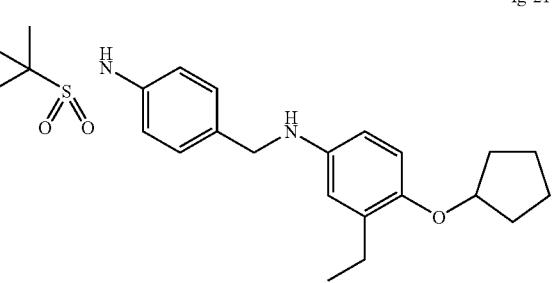
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Ig-221

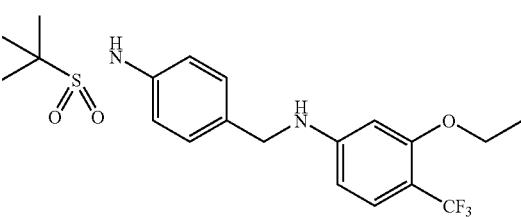
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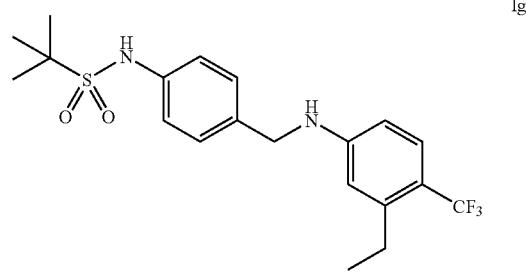
Ig-214

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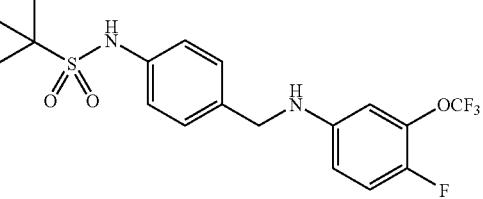
Ig-222

45



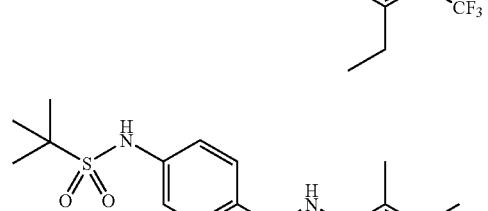
Ig-215

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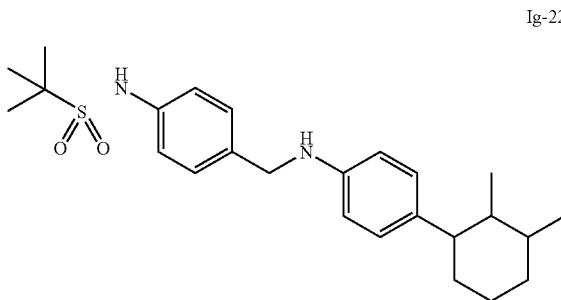
Ig-223

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Ig-216

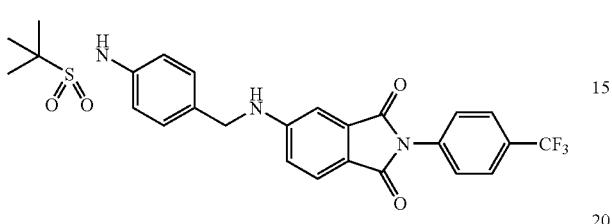
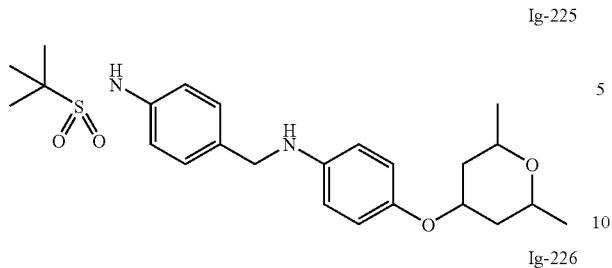
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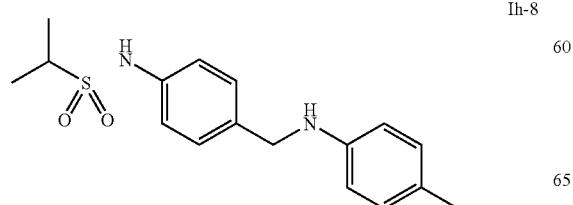
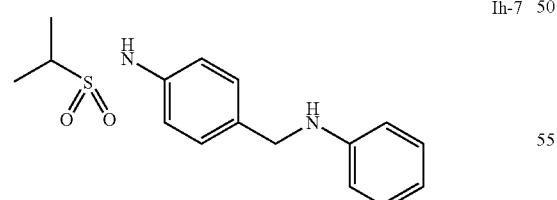
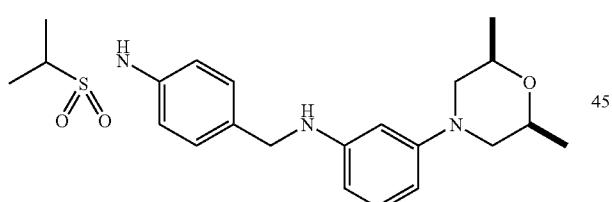
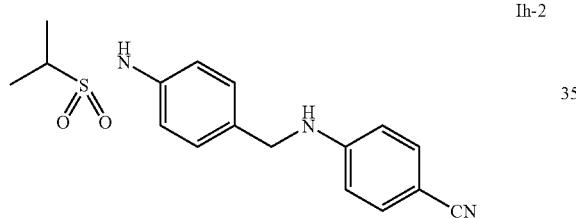
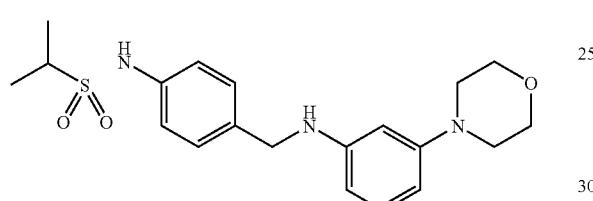
Ig-224

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317
-continued

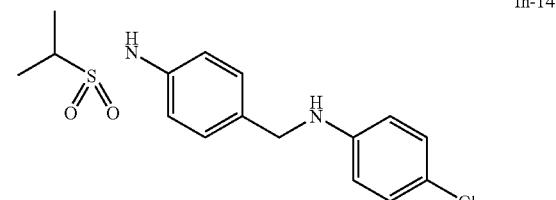
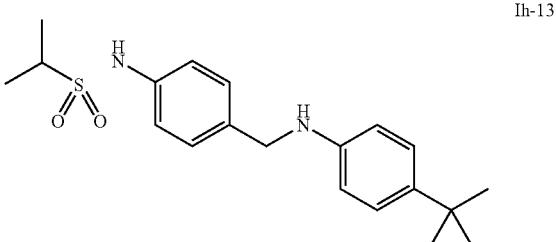
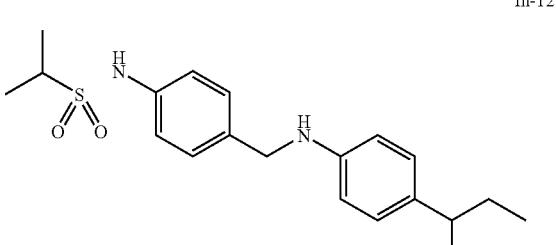
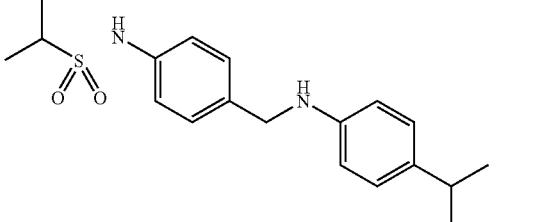
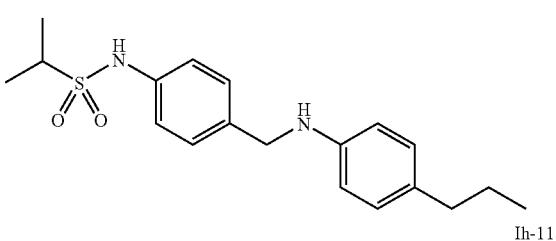
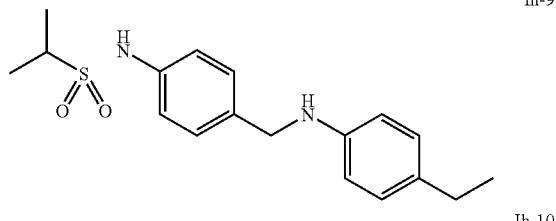


[Formula 155]



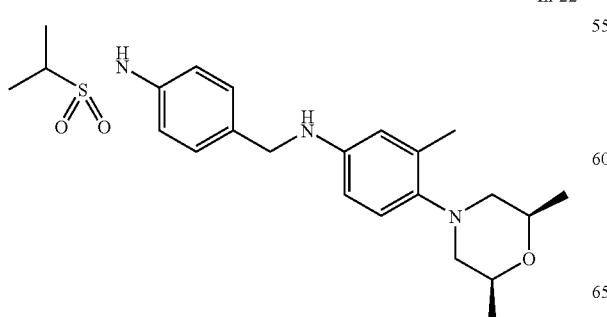
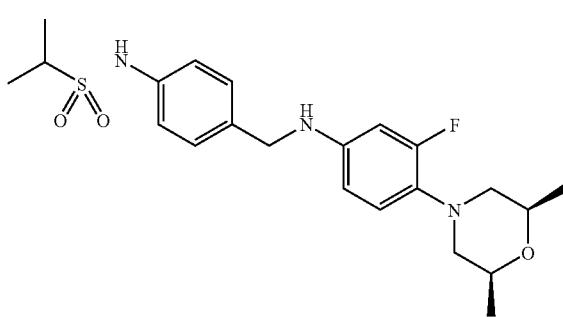
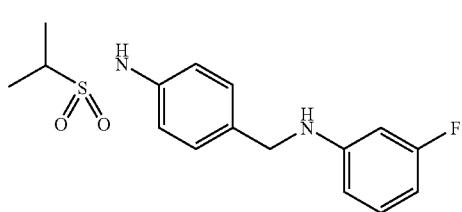
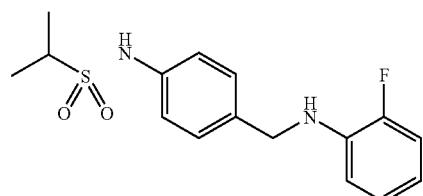
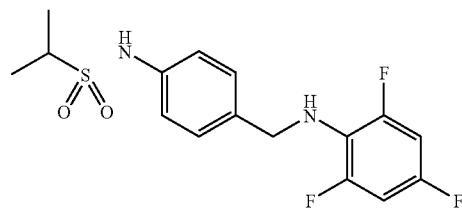
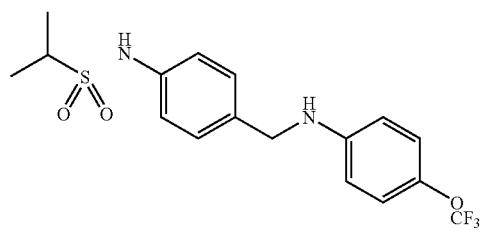
318
-continued

Ih-9

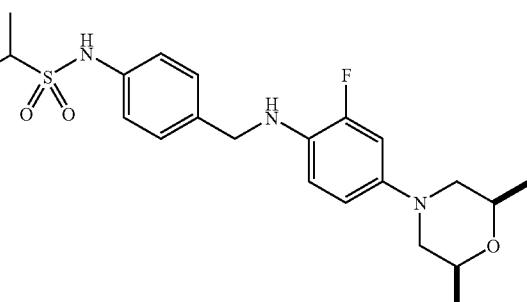
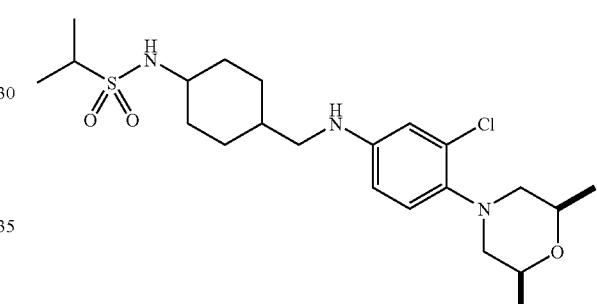
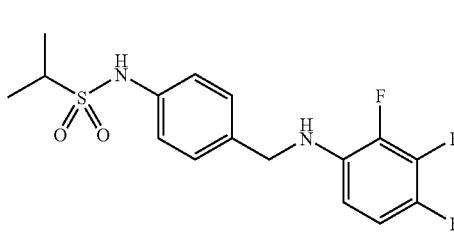
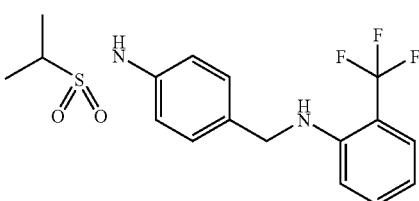


319

-continued

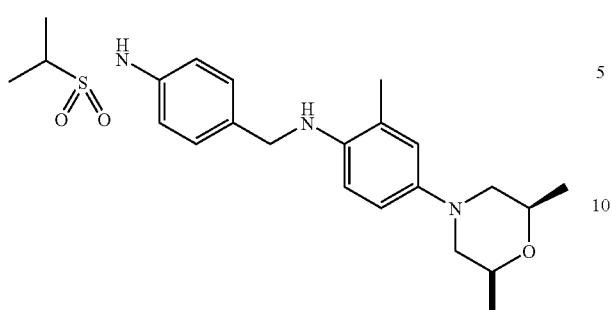
**320**

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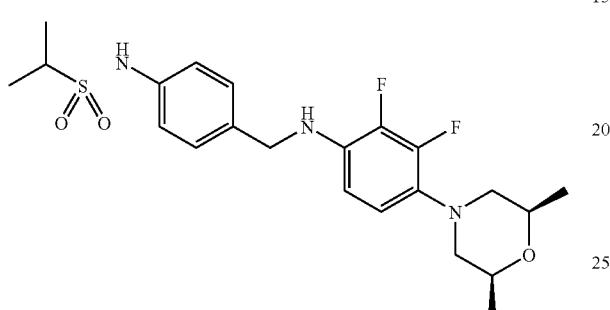
321

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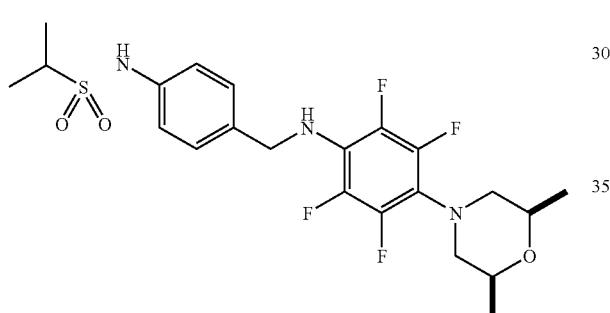


Ih-28

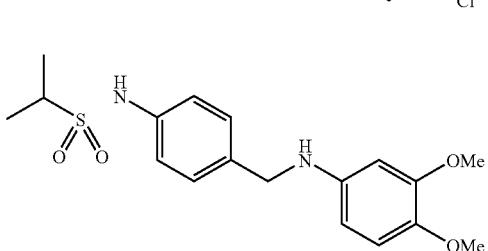
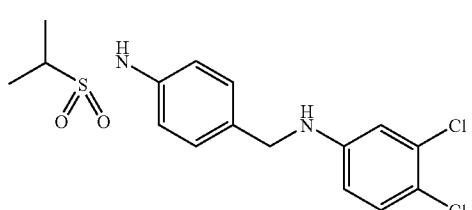
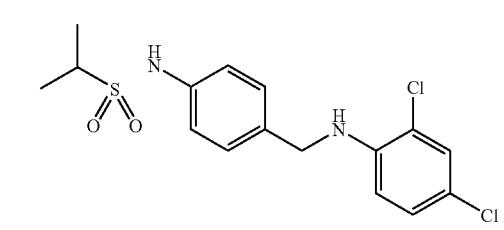
Ih-29 15



Ih-30



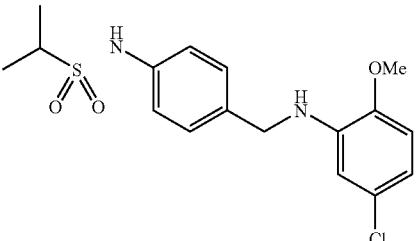
40



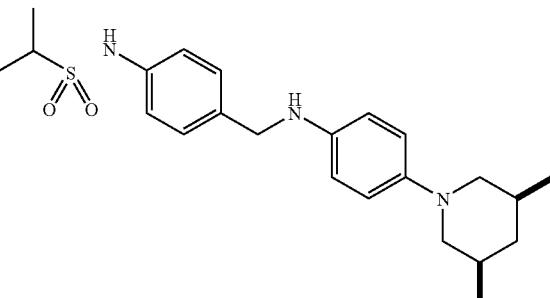
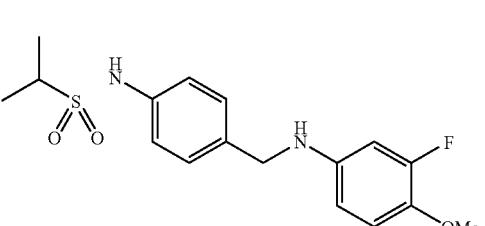
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322

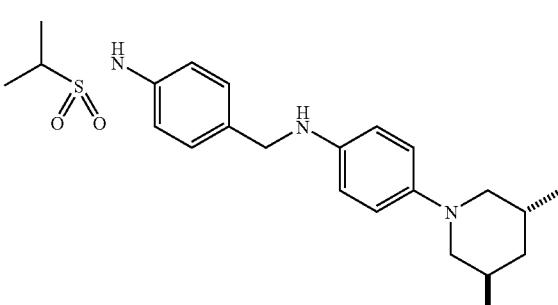
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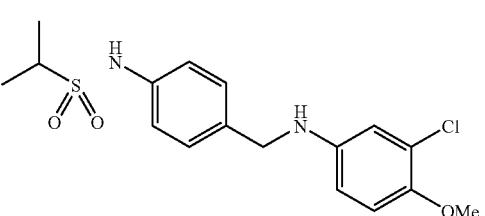
Jh-35



Ih-38

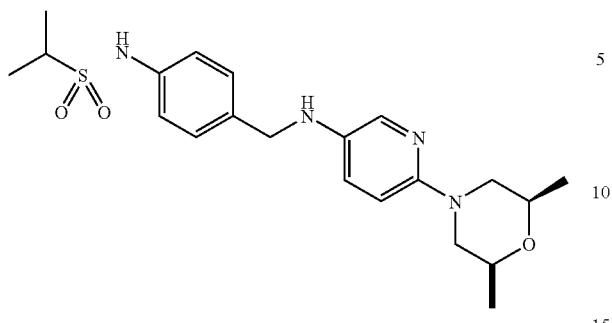


Ih-39



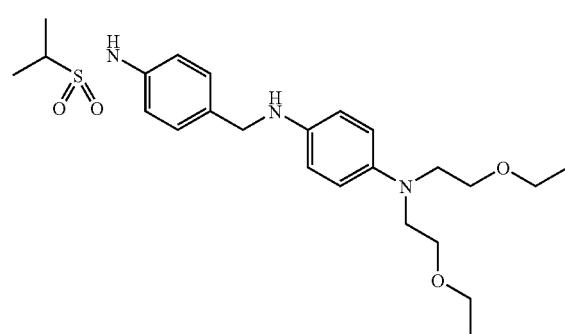
323

-continued

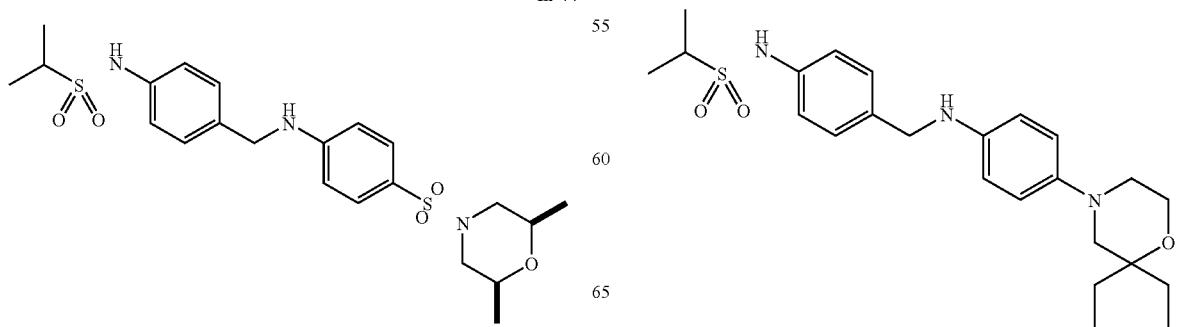
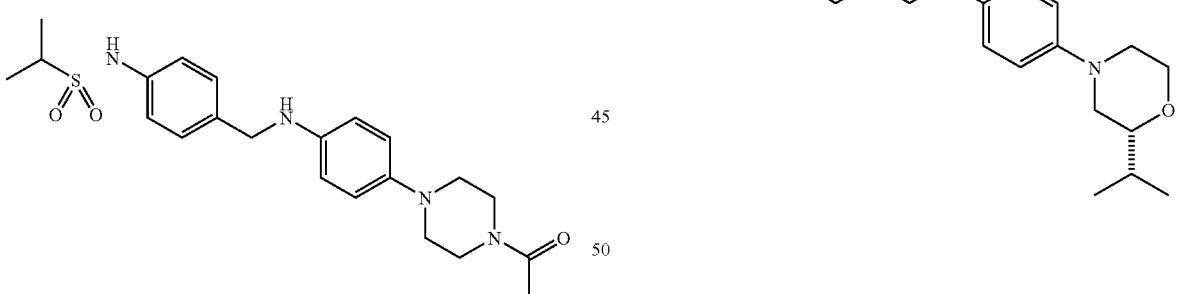
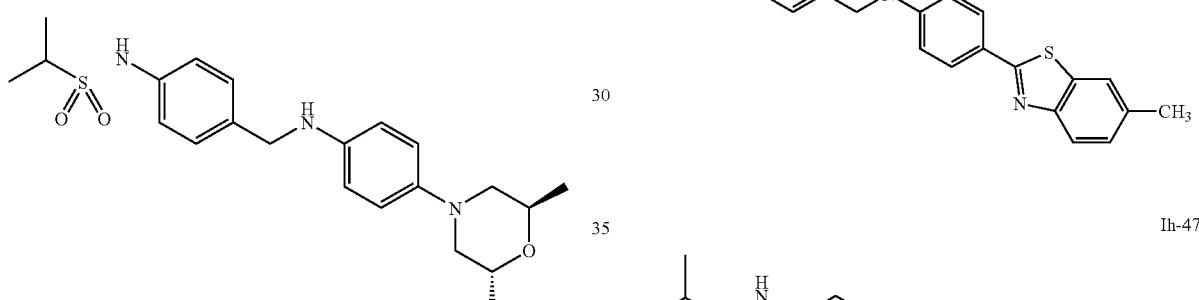
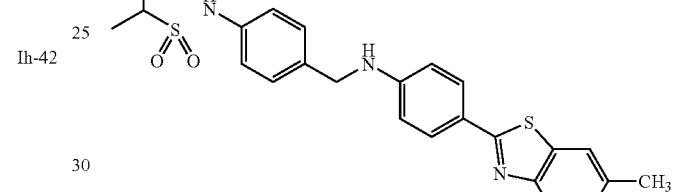
**324**

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Ih-45

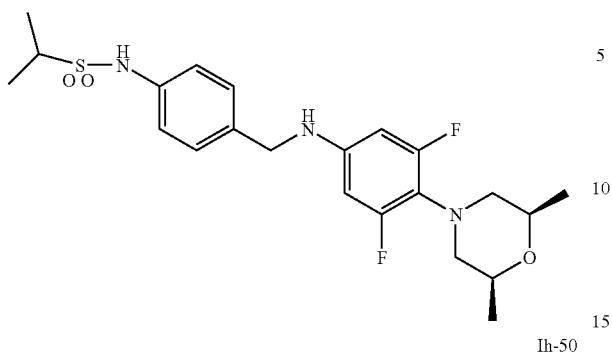


Ih-46

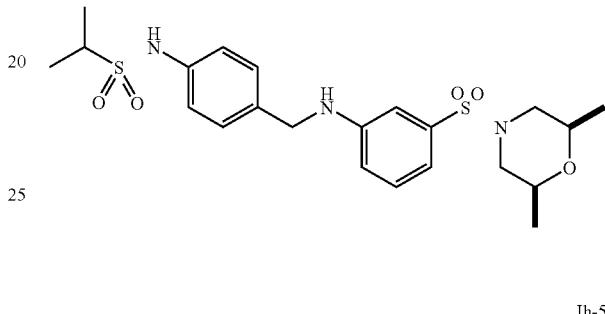
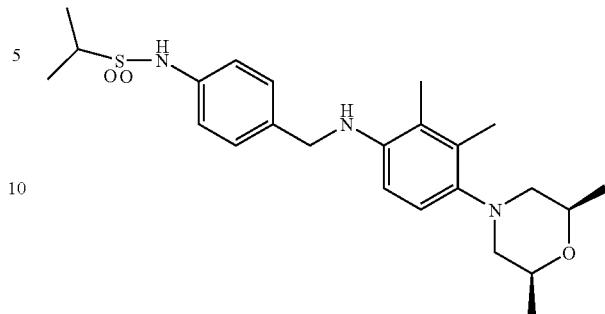


325

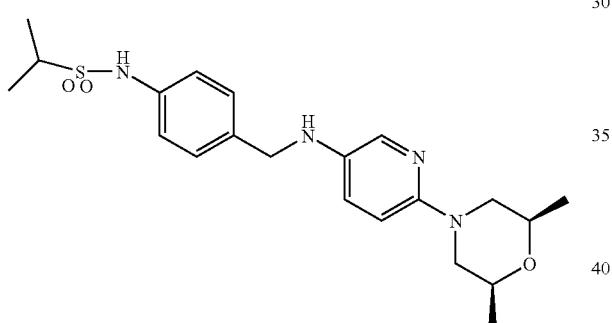
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**326**

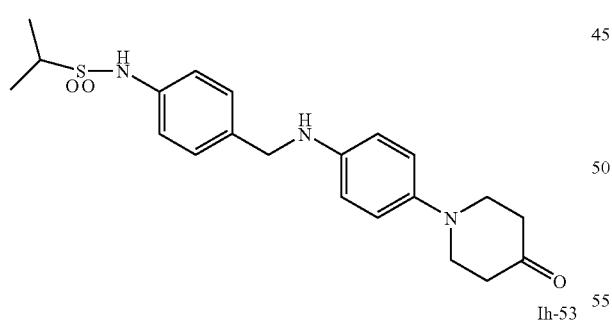
-continued



Ih-51

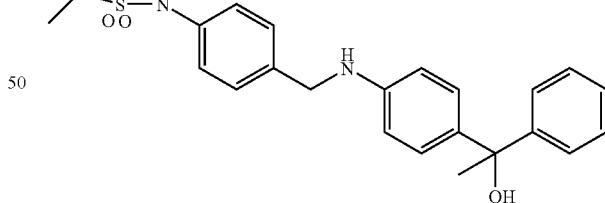


Ih-52



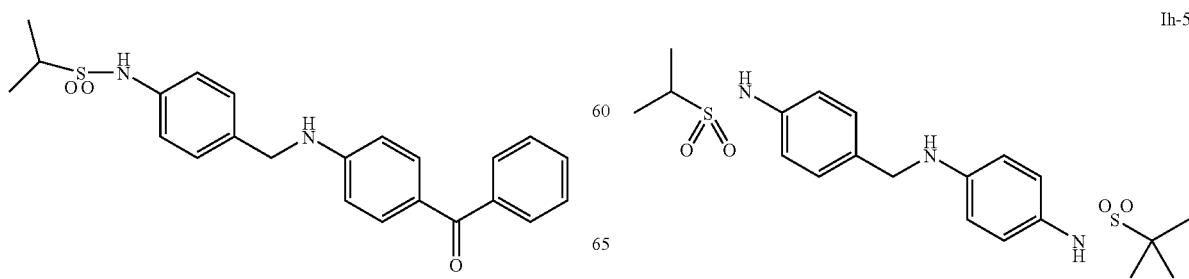
Ih-53

Ih-57



Ih-57

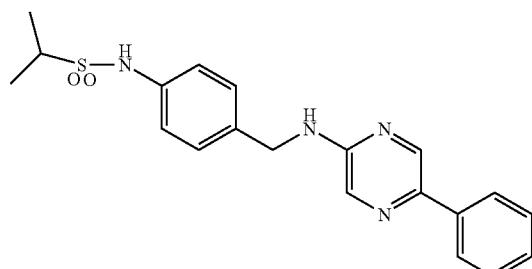
Ih-58



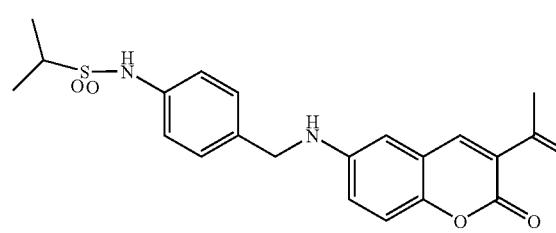
Ih-58

327

-continued

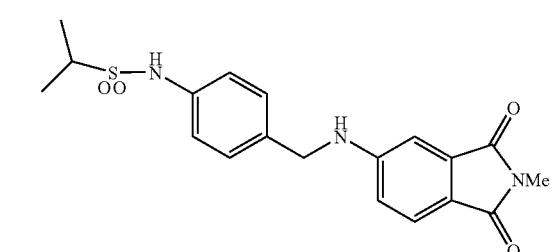


Ih-59



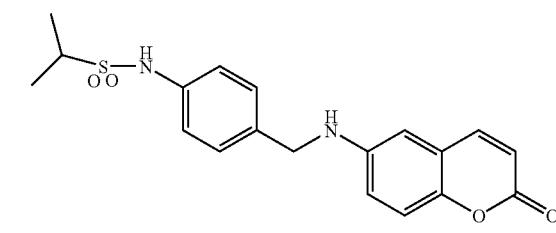
Ih-60

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Ih-61

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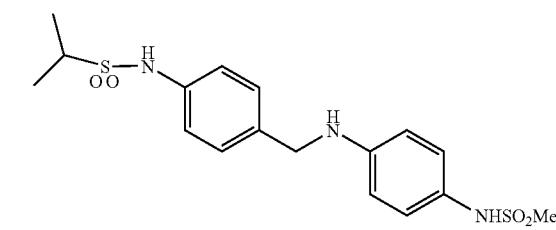


Ih-62

30

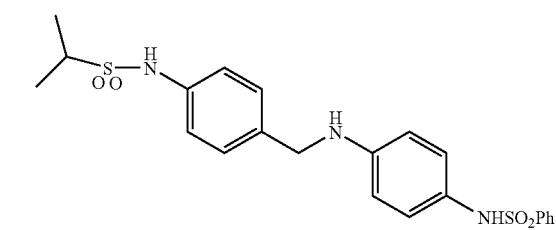
[Formula 158]

Ih-67



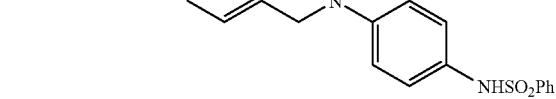
Ih-63

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Ih-64

60

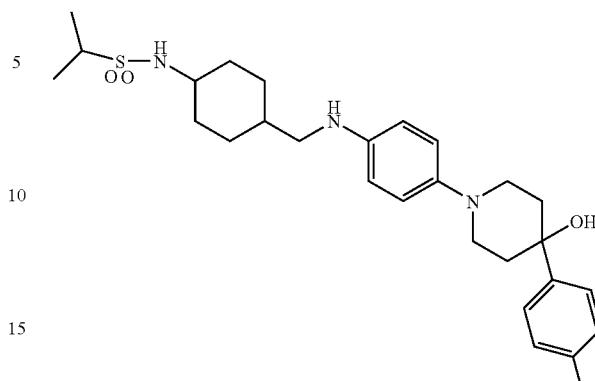


Ih-65

65

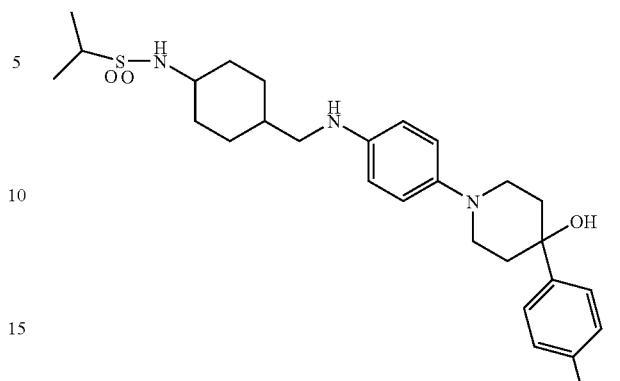
328

-continued

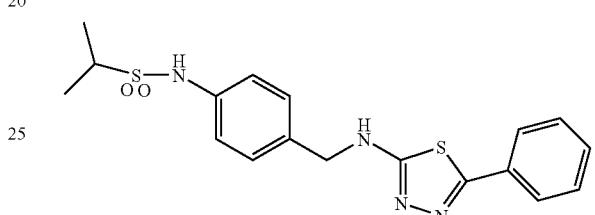


Ih-5

10



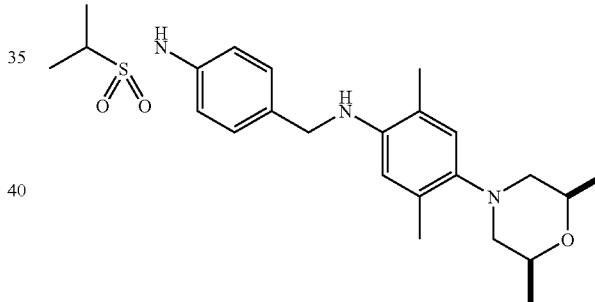
Ih-66



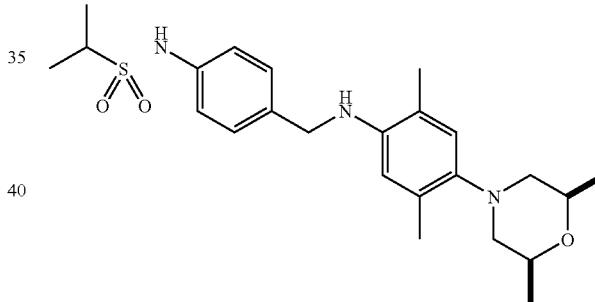
Ih-67

30

[Formula 158]

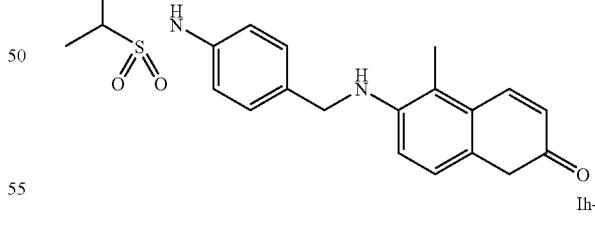


Ih-68



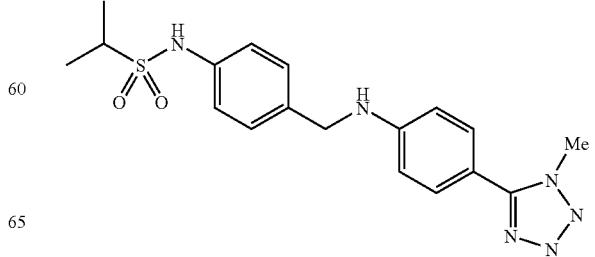
Ih-69

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Ih-64

55



Ih-65

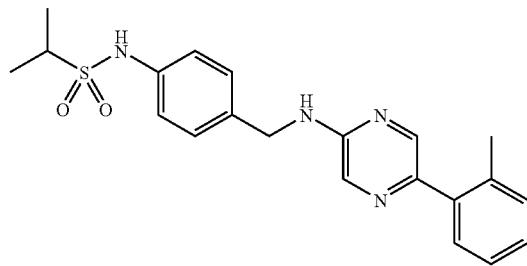
60

65

329

-continued

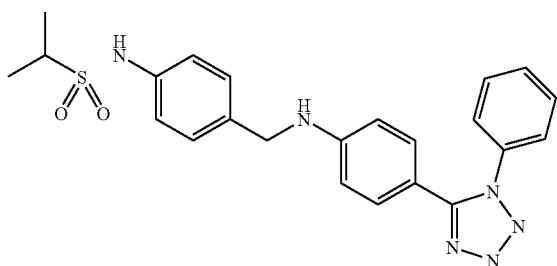
Ih-70



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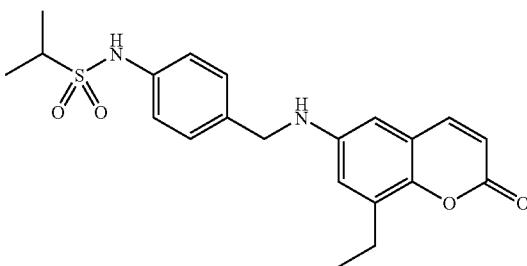
Ih-71



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Ih-72 25

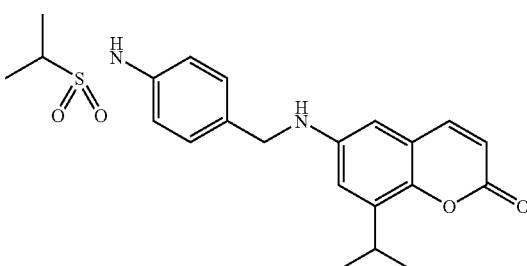


Ih-77

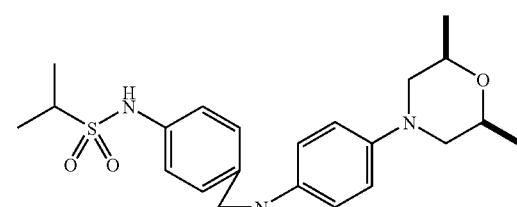
330

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Ih-77



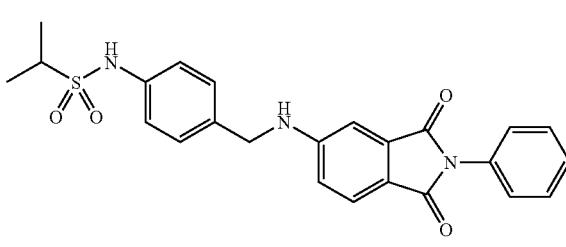
Ih-79



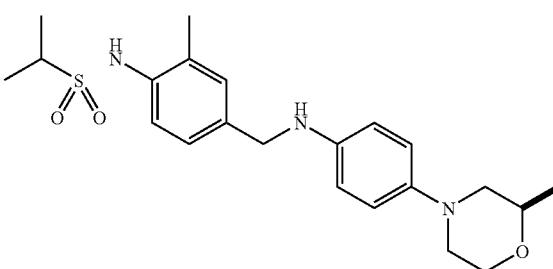
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35

Ih-74 35



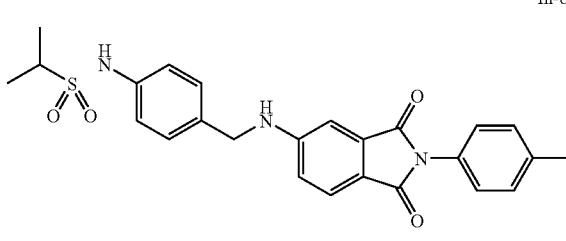
Ih-80



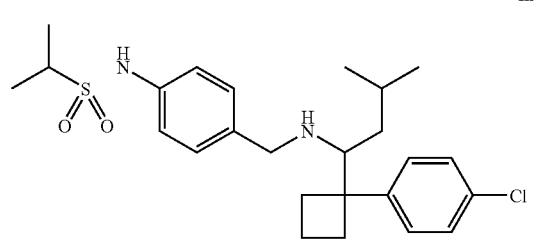
40

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Ih-75



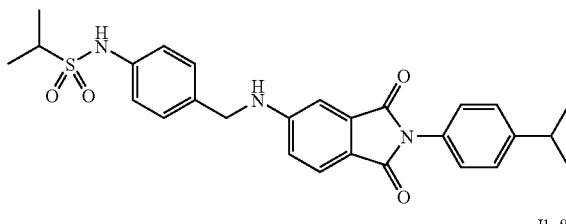
Ih-81



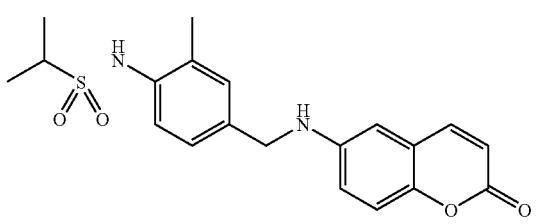
50

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Ih-76



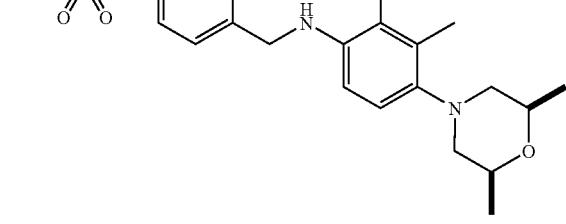
Ih-82



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65

Ih-65

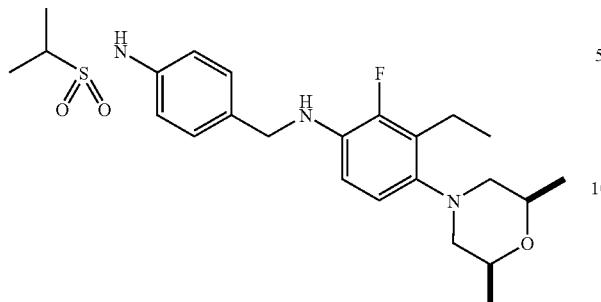


Ih-66

331

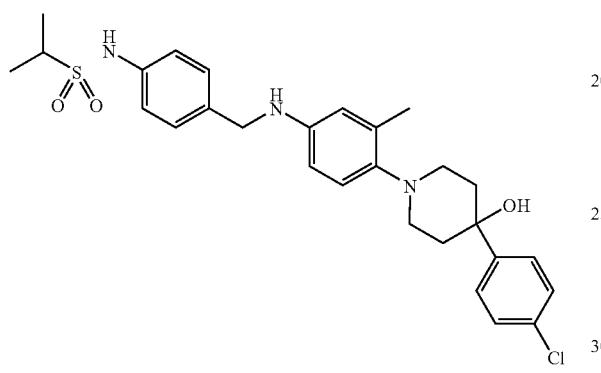
-continued

Ih-83



5

Ih-84

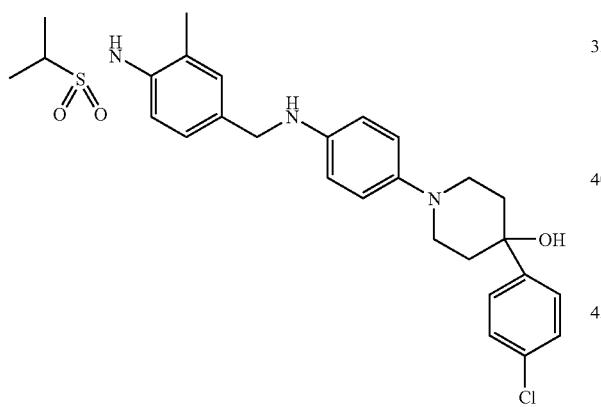


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[Formula 159]

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Ih-85



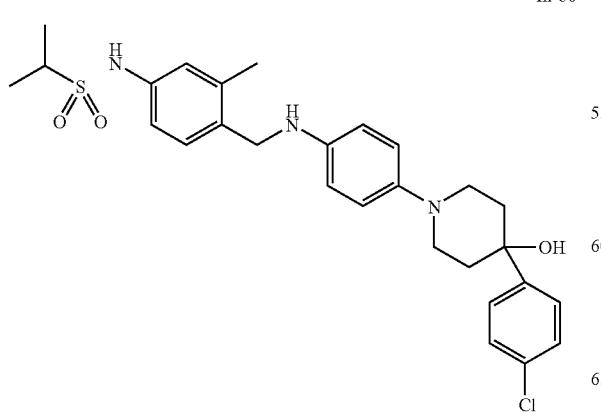
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Ih-86



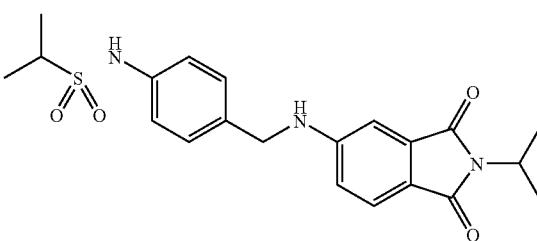
60

65

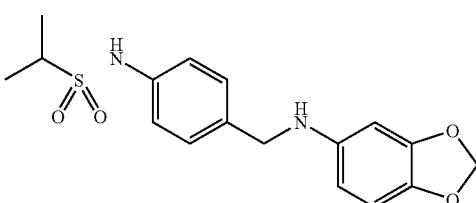
332

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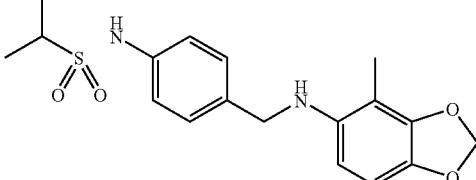
Ih-87



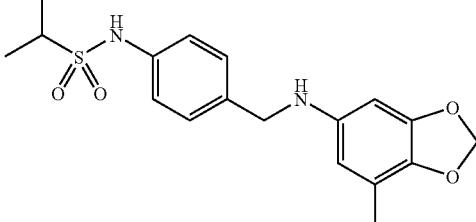
Ih-88



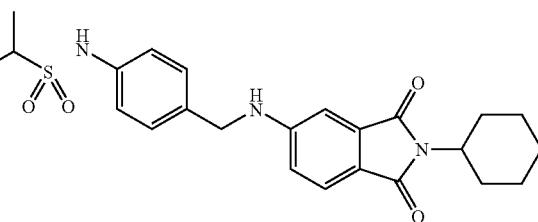
Ih-89



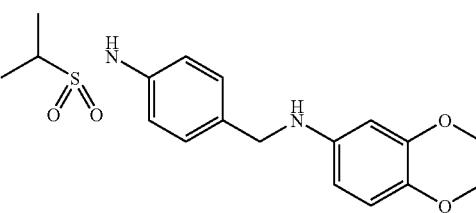
Ih-90



Ih-91

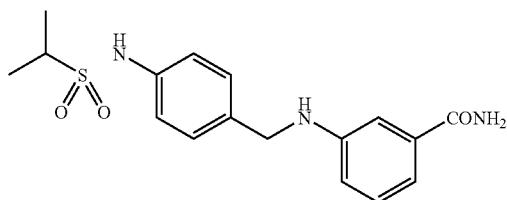


Ih-92

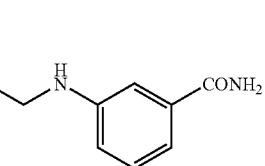


333

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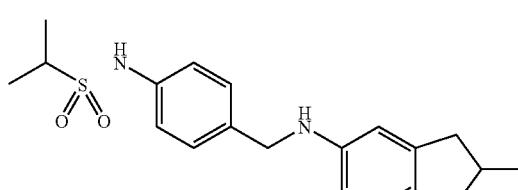


Ih-93



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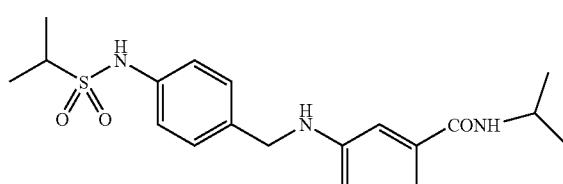
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Ih-94

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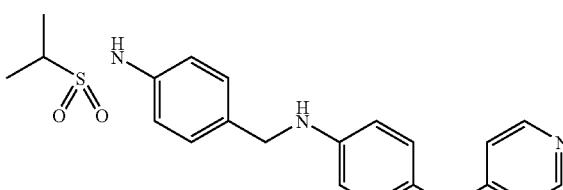
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Ih-95

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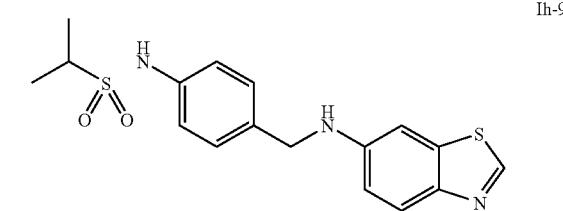
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Ih-96

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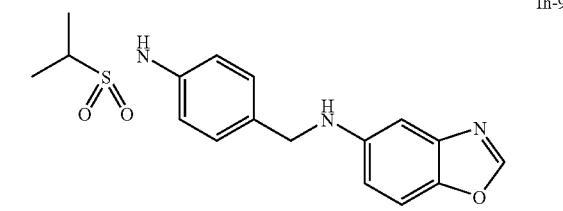
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Ih-97

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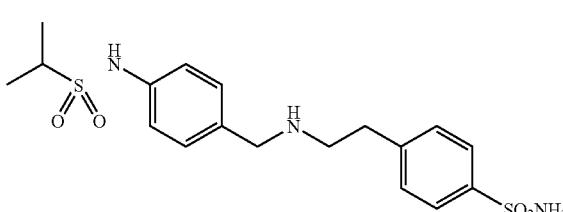
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Ih-98

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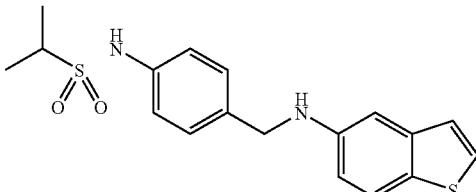
Ih-99

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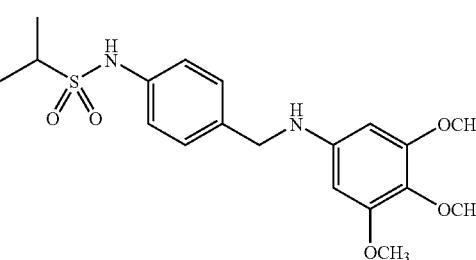
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334

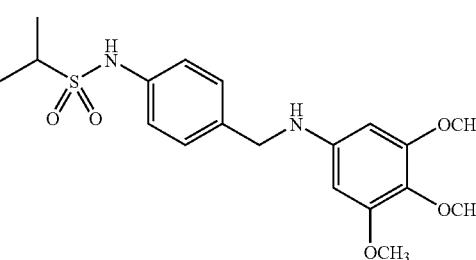
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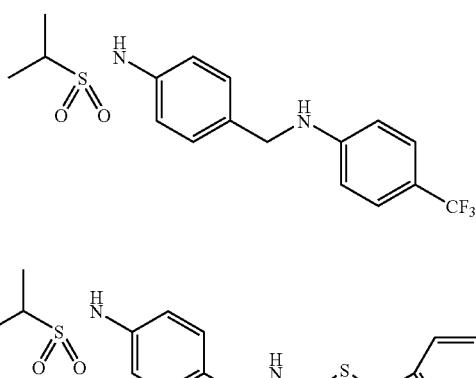
Ih-100



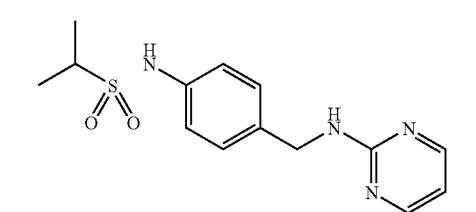
Ih-101



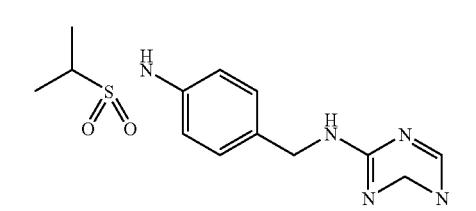
Ih-102



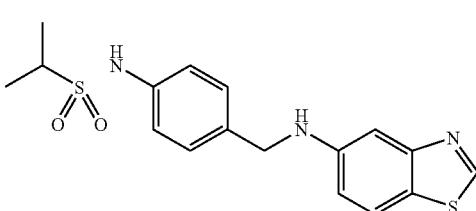
Ih-103



Ih-104



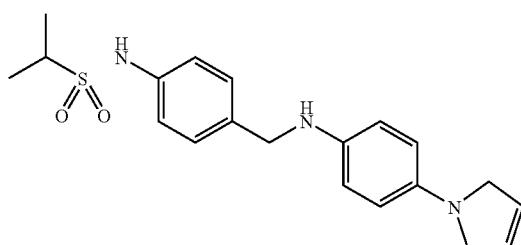
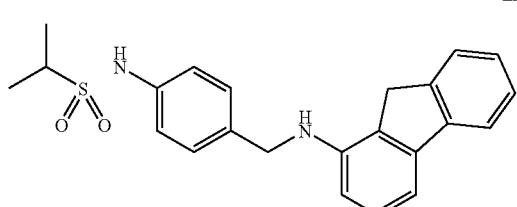
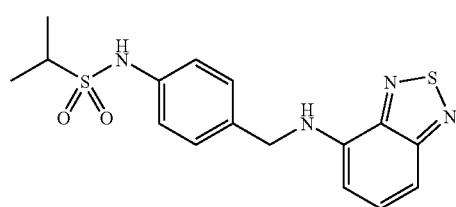
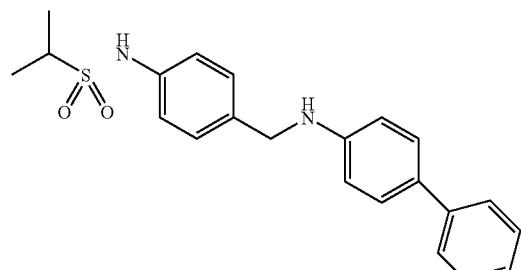
Ih-105



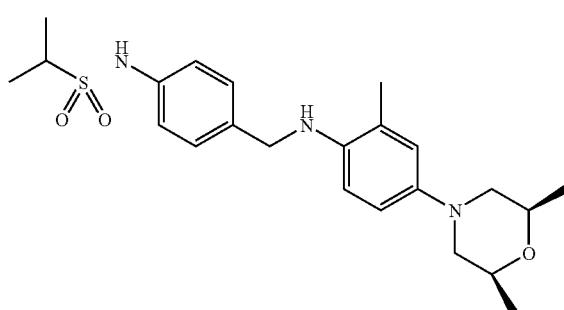
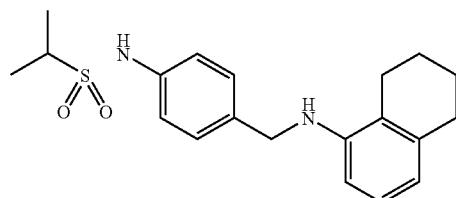
Ih-106

335

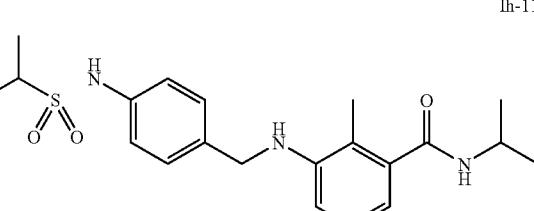
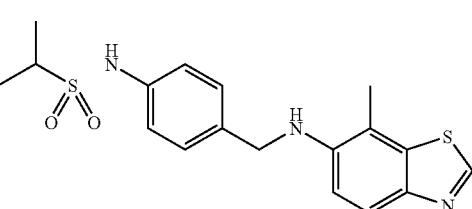
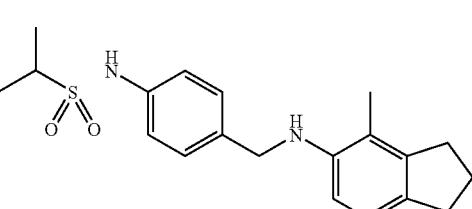
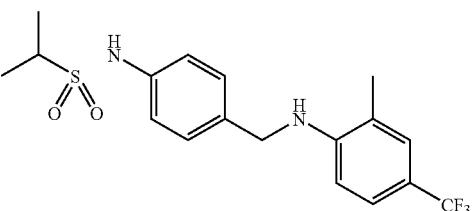
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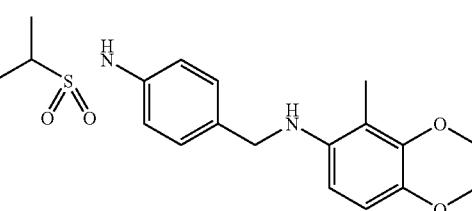
[Formula 160]

**336**

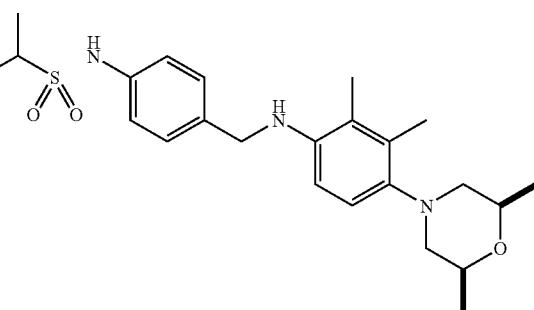
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Ih-117

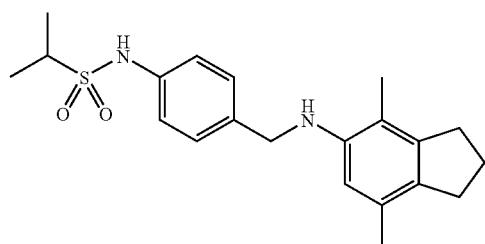


Ih-118

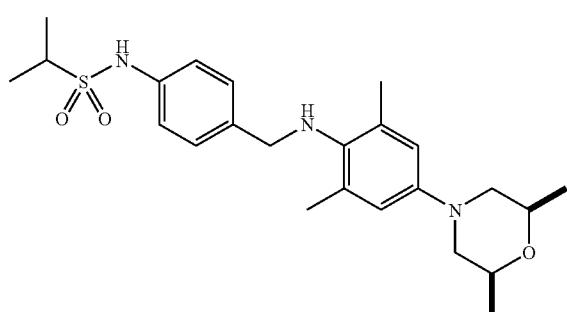


337

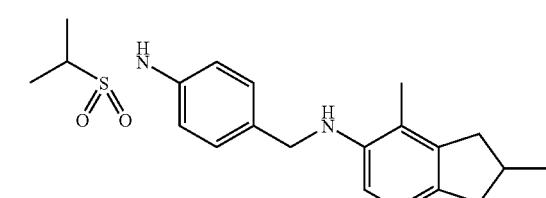
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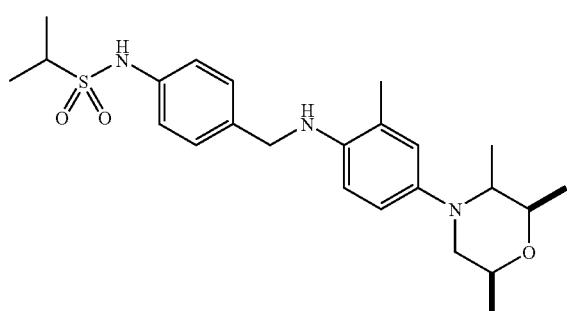
Ih-119



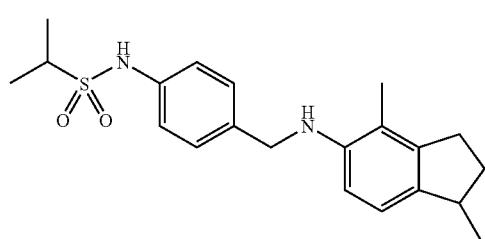
Ih-120 15



Ih-121 30



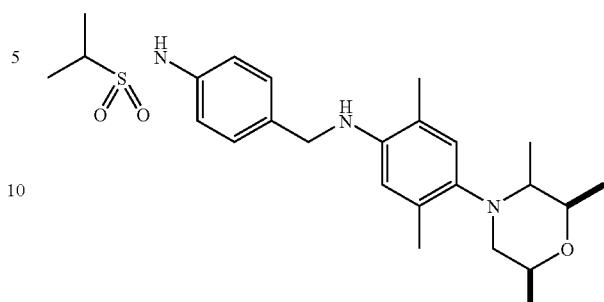
Ih-122



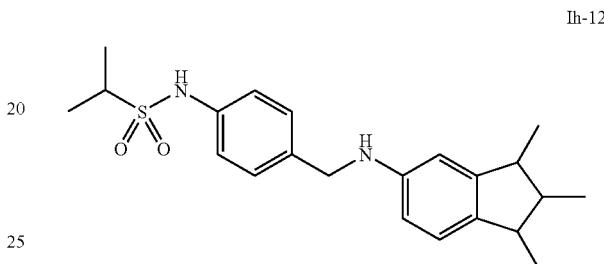
Ih-123

338

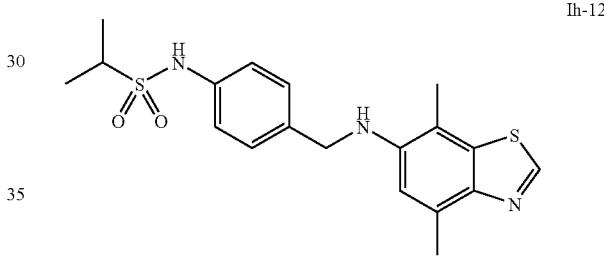
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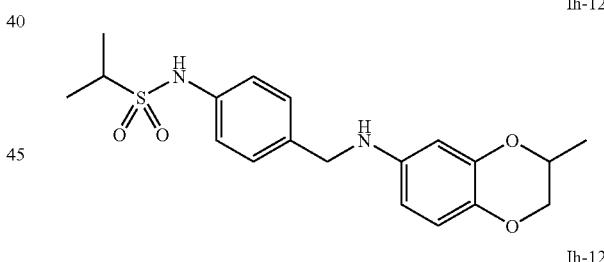
Ih-124



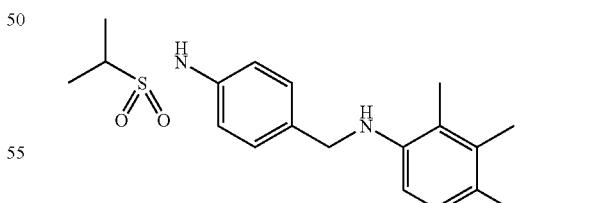
Ih-125



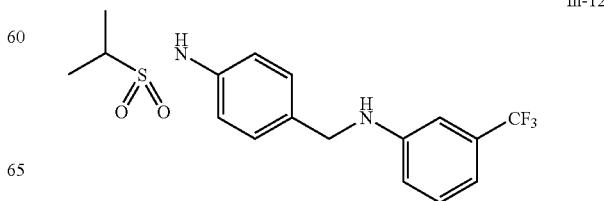
Ih-126



Ih-127



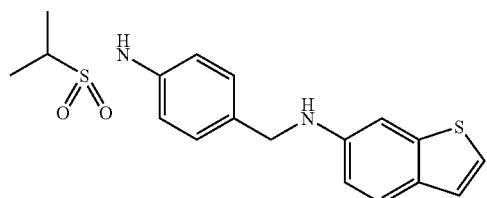
Ih-128



Ih-129

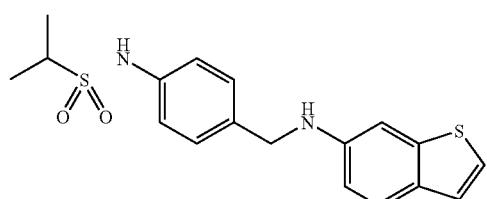
339

-continued



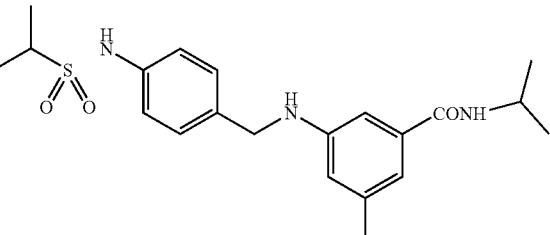
Ih-130

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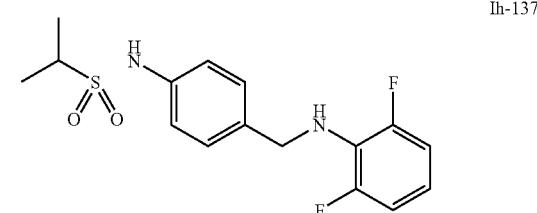
Ih-131

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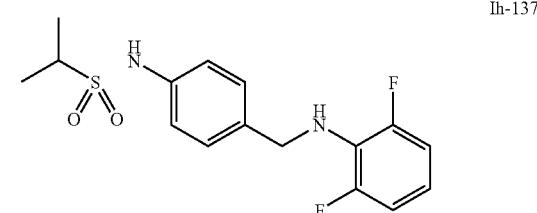
Ih-132

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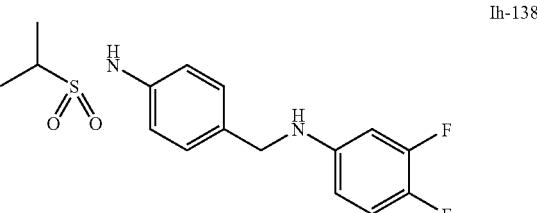
**340**

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Ih-136

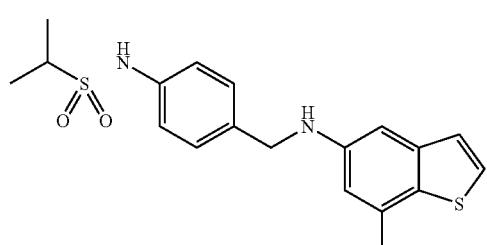


Ih-137



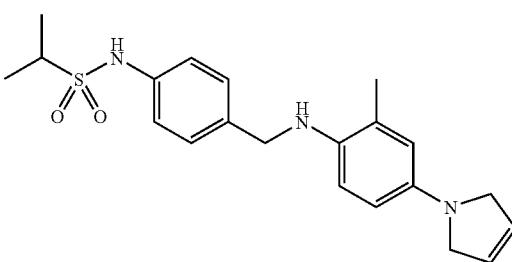
Ih-138

[Formula 161]

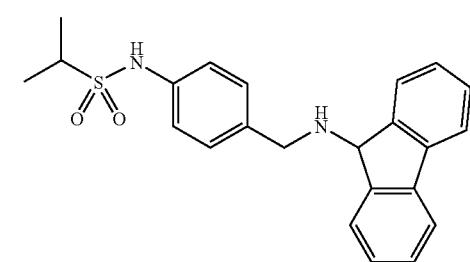


Ih-133

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Ih-139

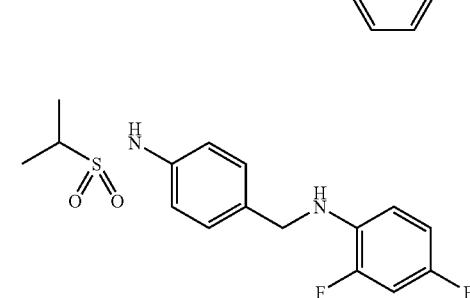


Ih-134

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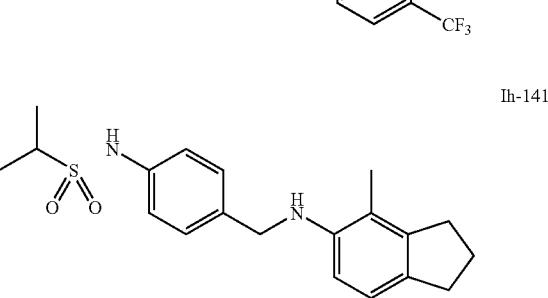


Ih-140



Ih-135

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Ih-141

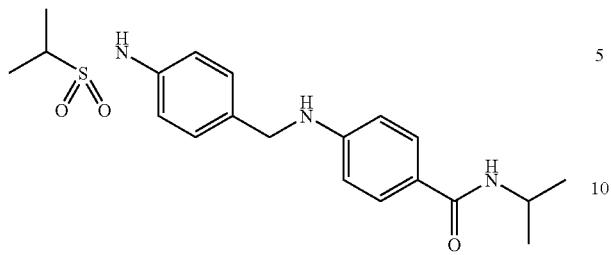
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341

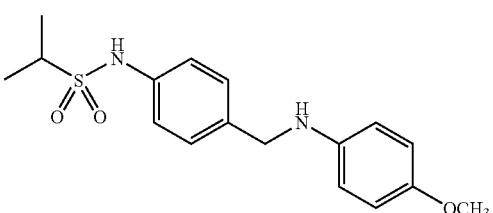
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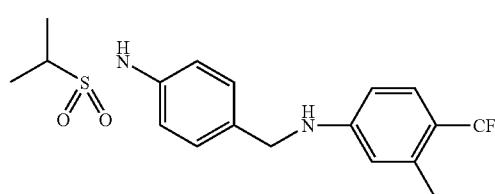
Ih-142

342

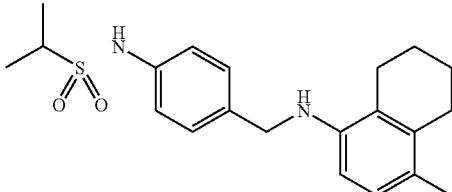
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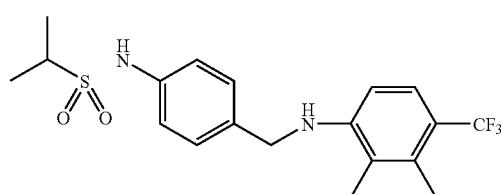
Ih-149



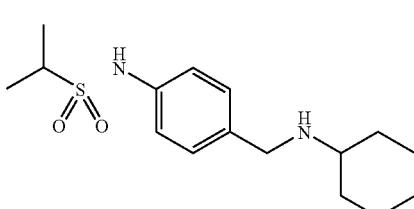
Ih-143



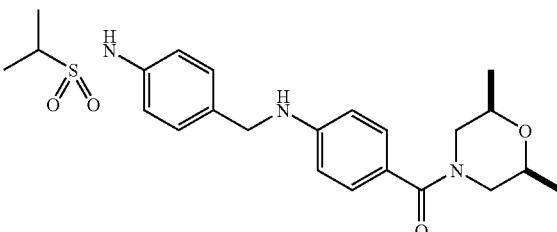
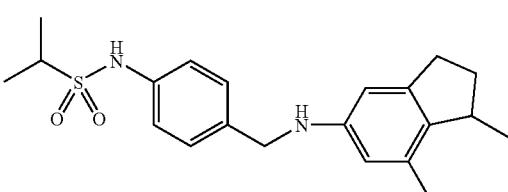
Ih-151



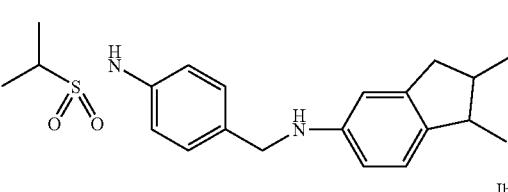
Ih-144 25



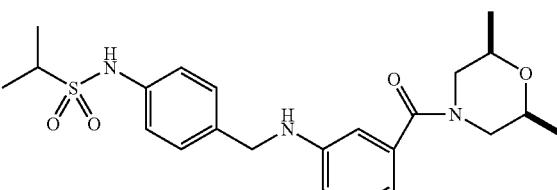
Jh-152



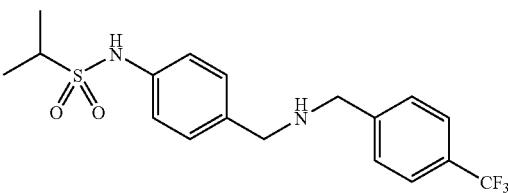
Jh-153



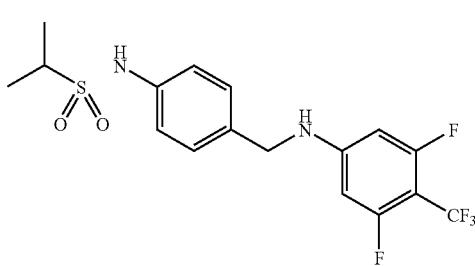
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Jh-154



55 [Formula 162]



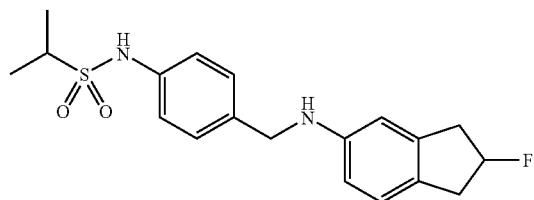
Jh-148

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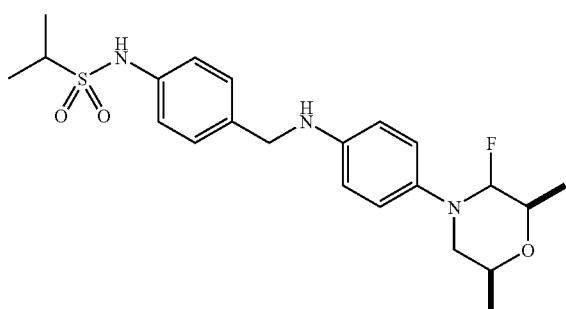
343

-continued

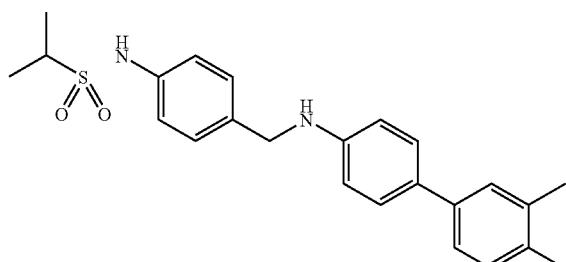
Ih-156

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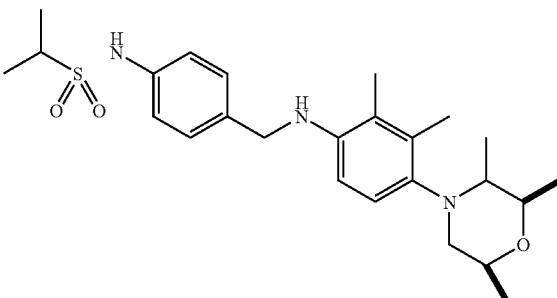
Ih-157

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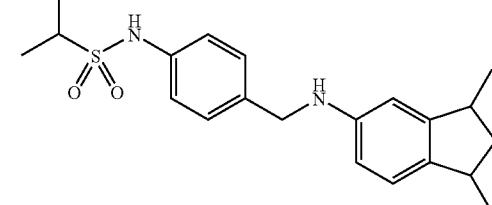
Ih-158

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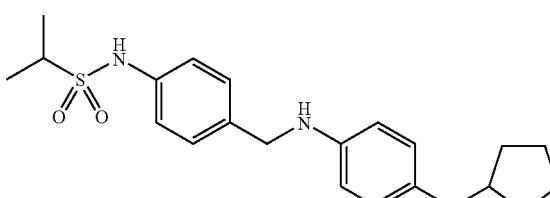
Ih-162



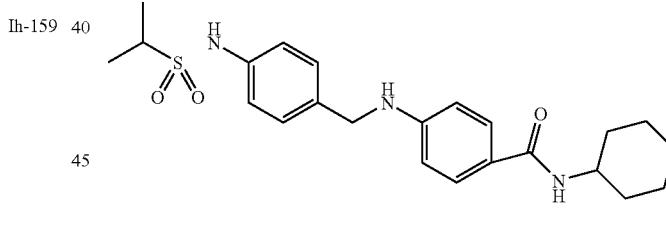
Ih-163



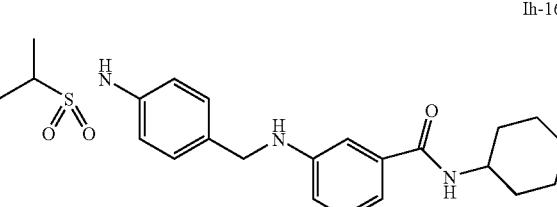
Ih-164



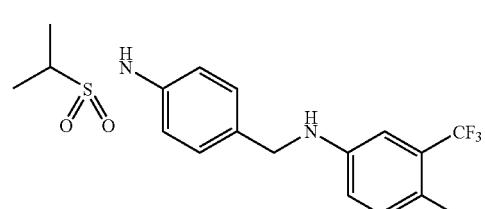
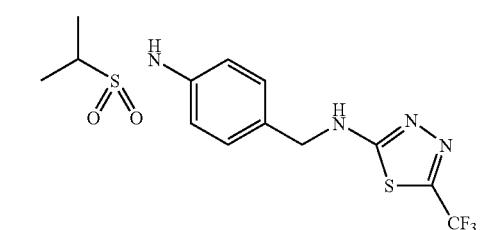
Ih-165

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Ih-166

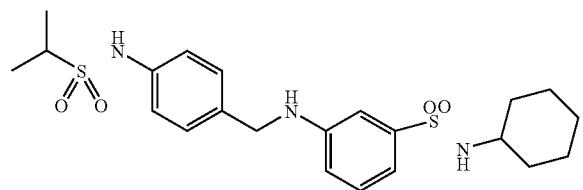
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Ih-161

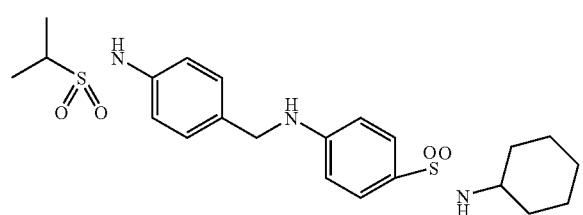
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345

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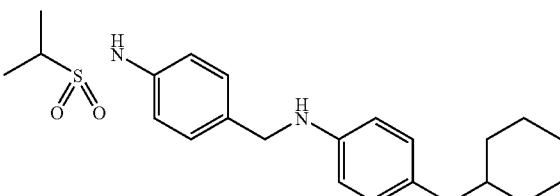
Ih-169

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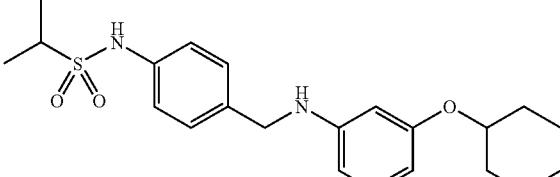
Ih-175

346

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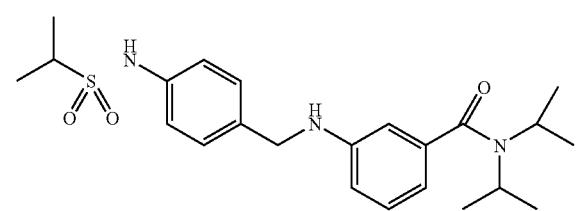


Ih-176



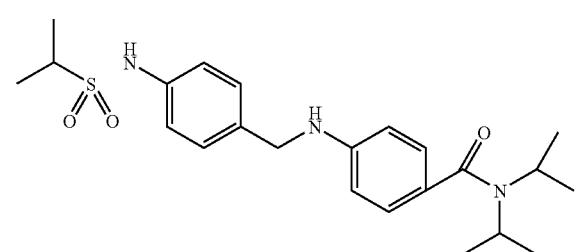
Ih-171

[Formula 163]

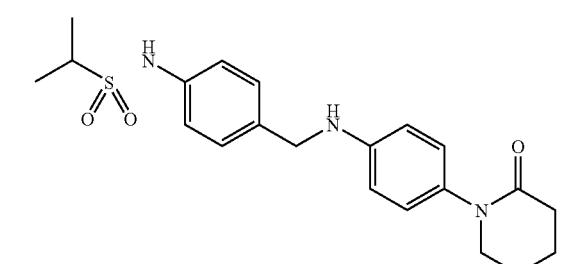
25
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Ih-177

Ih-172

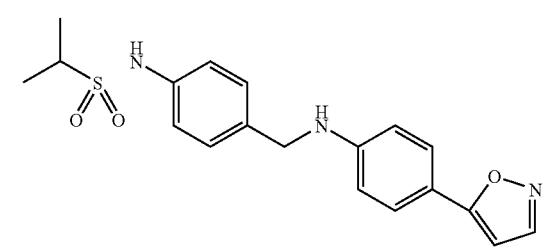
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Ih-178

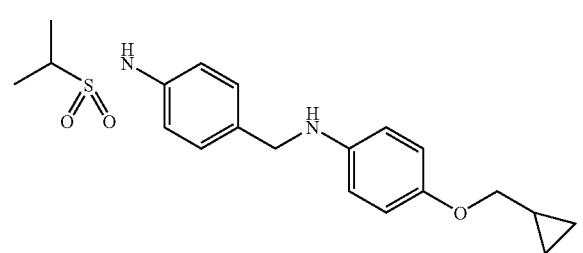
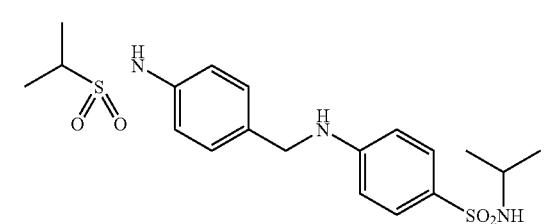


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Ih-179

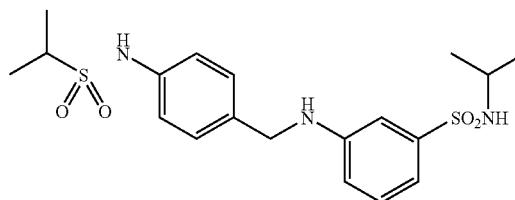
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Ih-180

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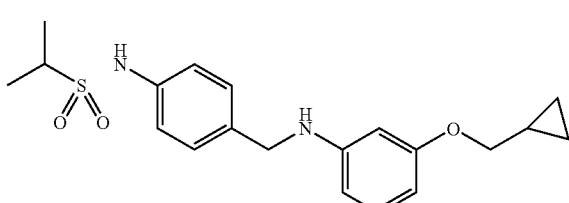
347
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Ih-181



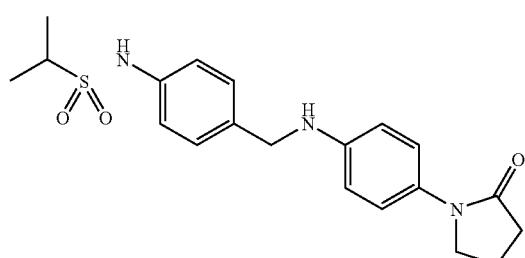
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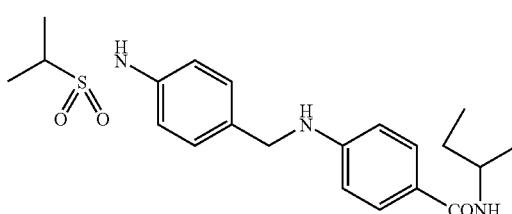
20



Ih-183

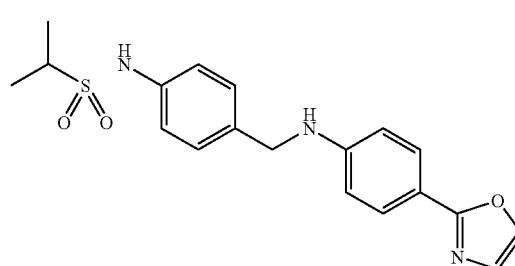
25

30



Ih-188

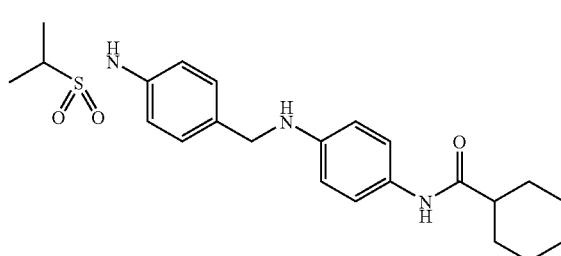
Ih-189



Ih-184

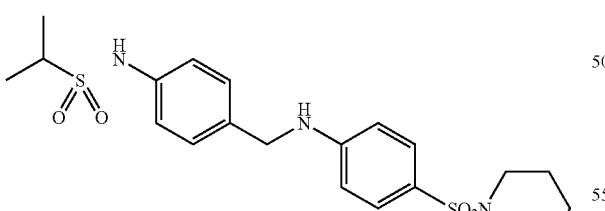
40

45



Ih-190

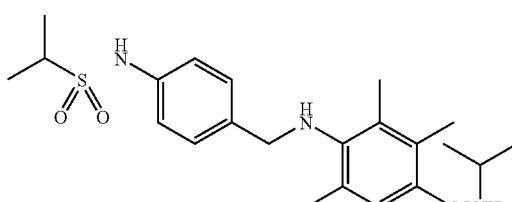
Ih-191



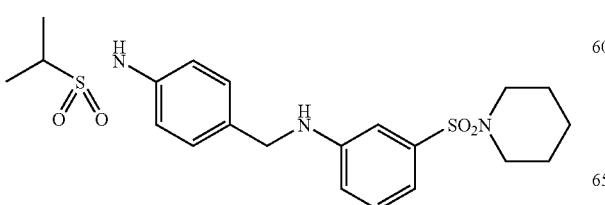
Ih-185

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55



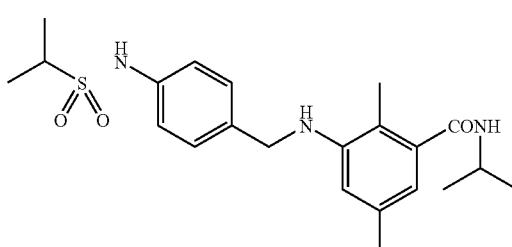
Ih-192



Ih-186

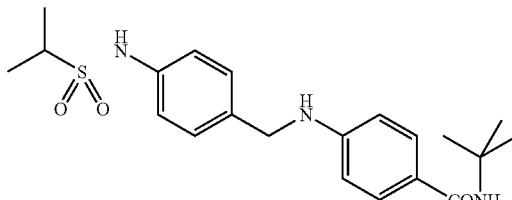
60

65



348
-continued

Ih-187

**348**

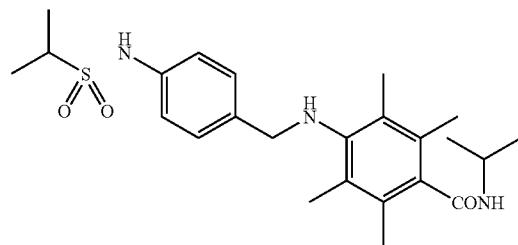
-continued

349

-continued

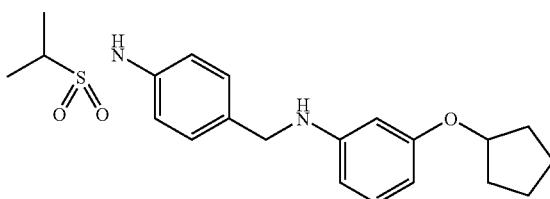
Ih-193

[Formula 164]

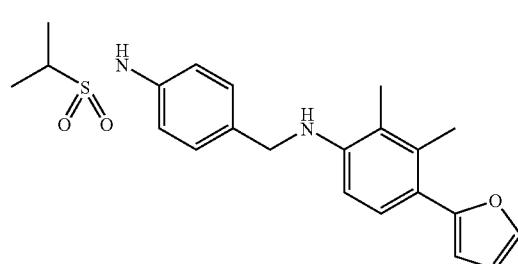
**350**

-continued

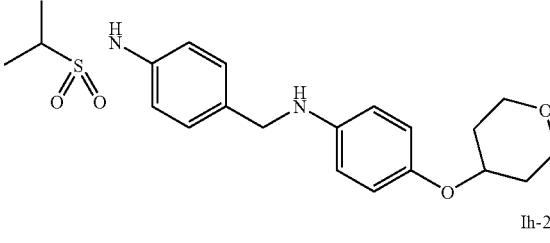
Ih-199



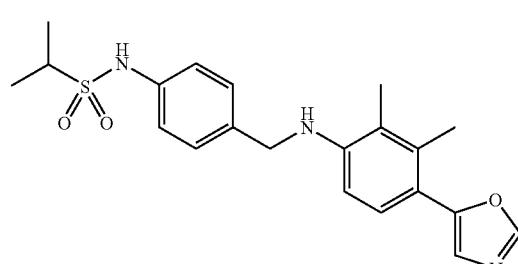
Ih-200



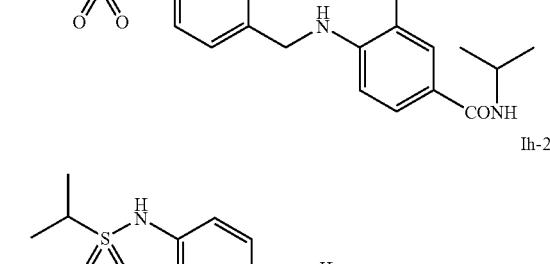
Ih-194



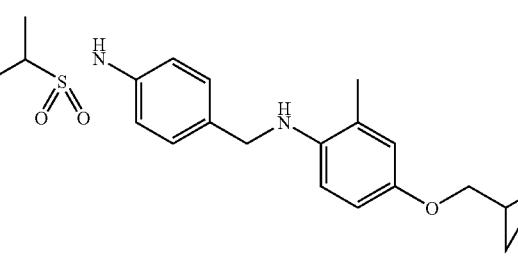
Ih-201



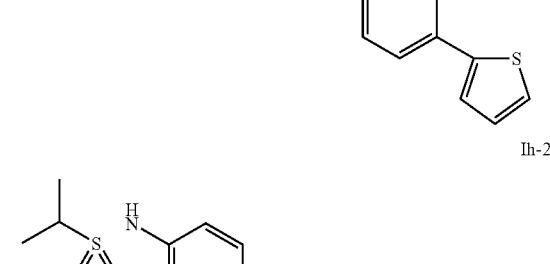
Ih-195



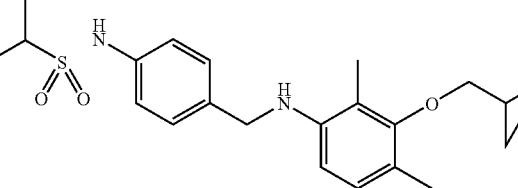
Ih-202



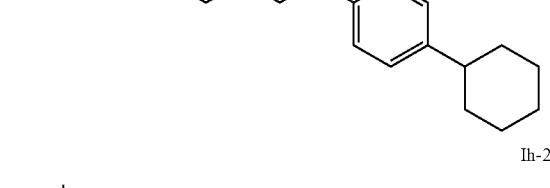
Ih-196



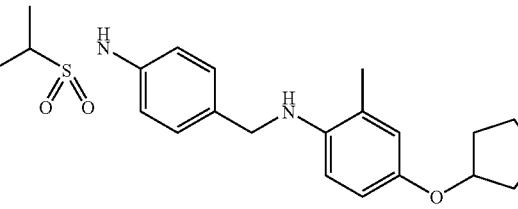
Ih-203



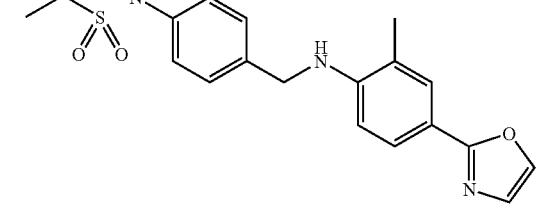
Ih-197



Ih-204



Ih-198

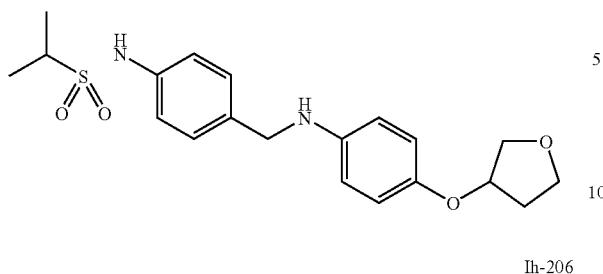


Ih-205

351

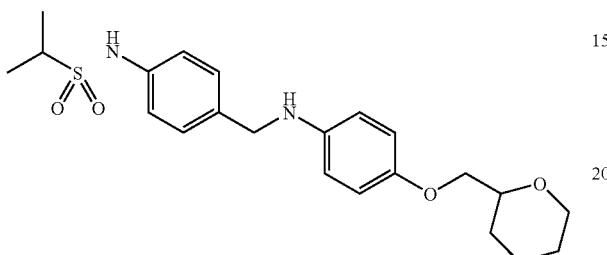
-continued

Ih-205



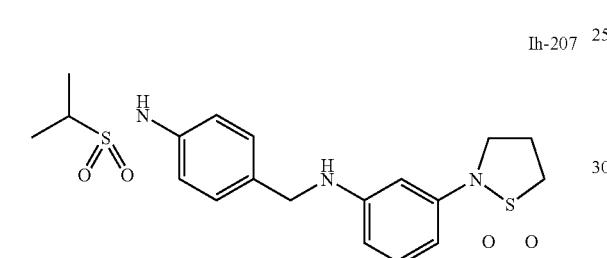
5

Ih-206



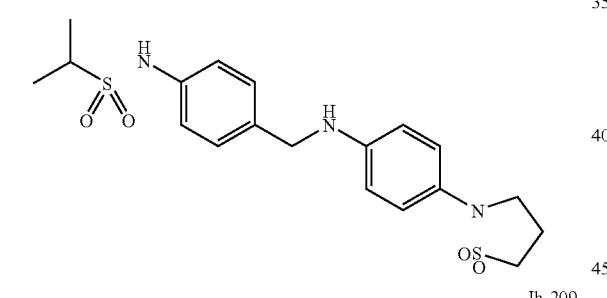
15

Ih-207



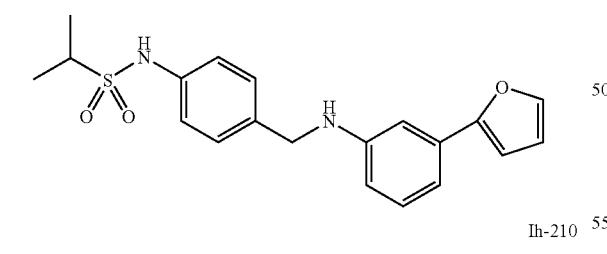
25

Ih-208



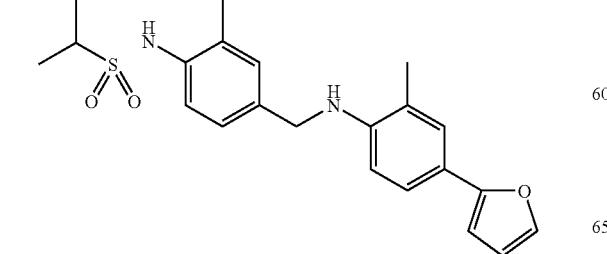
35

Ih-209



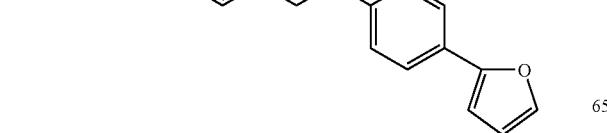
40

Ih-210



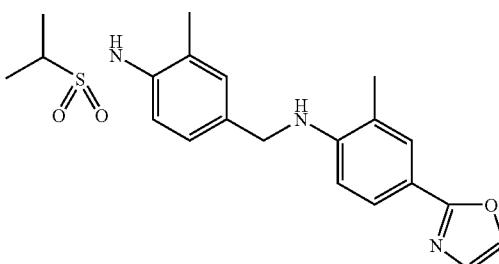
50

Ih-211

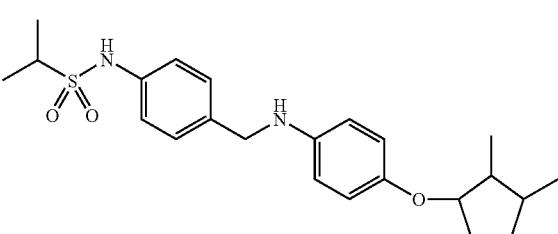
**352**

-continued

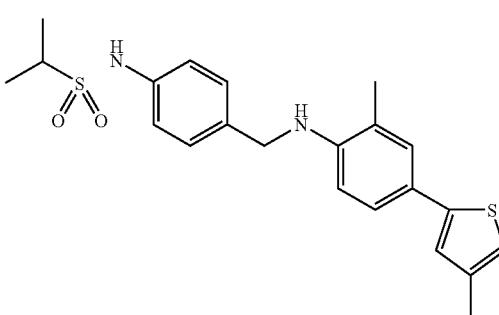
Ih-212



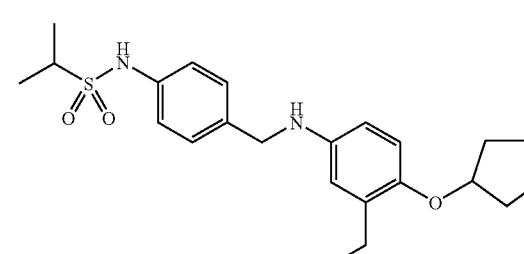
5



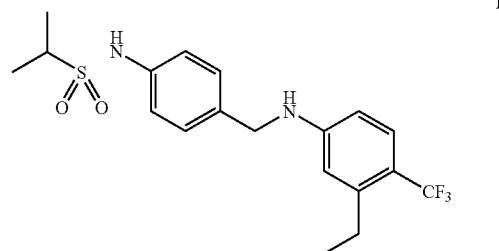
15



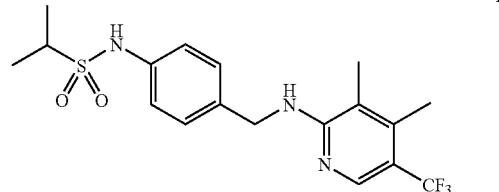
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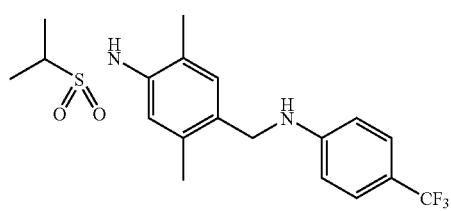
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353

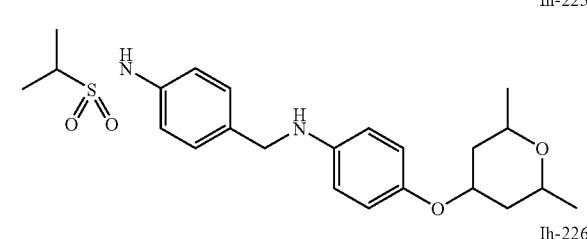
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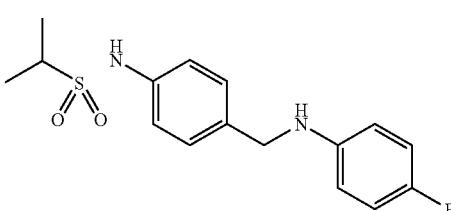
Ih-219

354

-continued

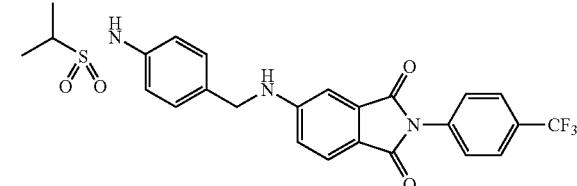


Ih-225

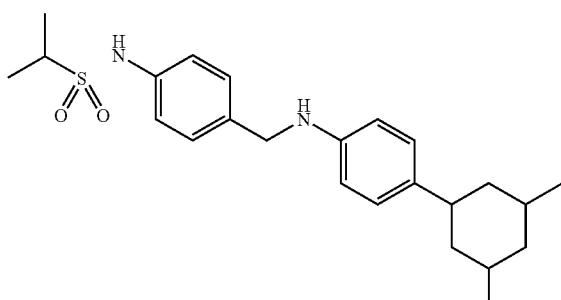


Ih-220

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Ih-221

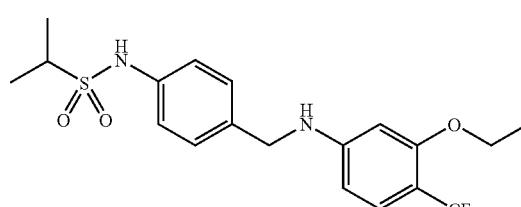


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Compound I-72

[Formula 165]

Ih-222



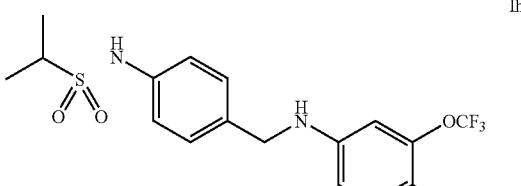
40

Ih-223

¹H-NMR (DMSO-d₆) δ: 0.90-1.05 (m, 2H), 1.05-1.15 (m, 6H), 1.25 (s, 9H), 1.15-1.32 (m, 3H), 1.41 (m, 1H), 1.75-1.98 (m, 4H), 2.11 (m, 1H), 2.58-3.38 (m, 5H), 3.58-3.76 (m, 2H), 5.17 (m, 1H), 6.25-6.92 (m, 5H) Melting point: 147 to 149°C.

Compound Ia-140

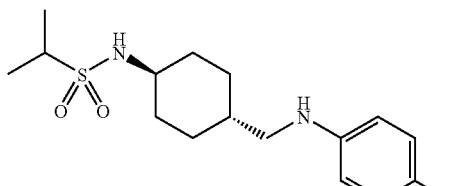
[Formula 166]



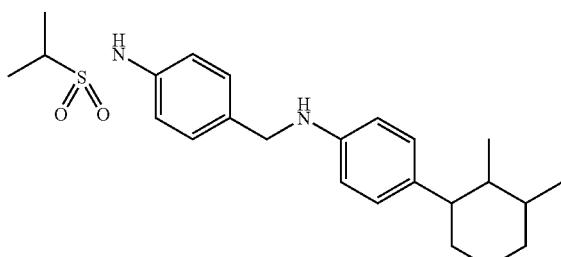
50

Ih-224

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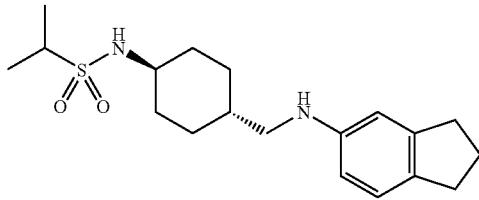


¹H-NMR (CDCl₃) δ: 1.02-1.20 (m, 2H), 1.17-1.32 (m, 2H), 1.37 (d, 6H, J=6.9 Hz), 1.46-1.70 (m, 4H), 1.86-1.95 (m, 2H), 2.08-2.18 (m, 2H), 3.01 (d, 2H, J=6.9 Hz), 3.13 (m, 1H), 3.25 (m, 1H), 3.87 (d, 1H, J=8.4 Hz), 6.61 (d, 2H, J=8.7 Hz), 7.39 (d, 2H, J=8.7 Hz)

355

Compound Ia-141

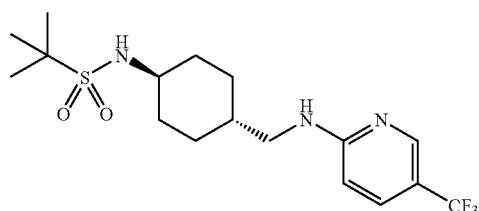
[Formula 167]



¹H-NMR (CDCl₃) δ: 1.00-1.30 (m, 4H), 1.37 (d, 6H, J=6.9 Hz), 1.59 (m, 1H), 1.87-1.98 (m, 2H), 1.99-2.18 (m, 5H), 2.85 (q, 3H, J=7.5 Hz), 2.97 (d, 2H, J=6.9 Hz), 3.12 (m, 1H), 3.23 (m, 1H), 3.88 (d, 1H, J=8.1 Hz), 6.53 (d, 1H, J=7.8 Hz), 6.63 (brs, 1H), 7.04 (d, 1H, J=7.8 Hz) Mass: 351[M+H]⁺

Compound Ia-178

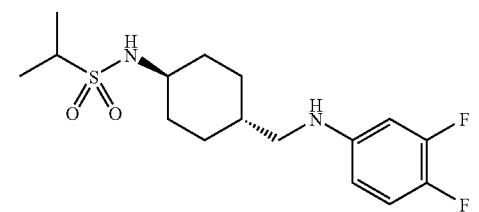
[Formula 168]



¹H-NMR (CDCl₃) δ: 1.08-1.36 (m, 4H), 1.39 (s, 9H), 1.59 (m, 1H), 1.90-1.99 (m, 2H), 2.16-2.26 (m, 2H), 3.17-3.34 (m, 3H), 3.69 (d, 1H, J=9.3 Hz), 6.68 (d, 1H, J=9.3 Hz), 7.77 (dd, 1H, J=2.1 Hz and 9.3 Hz), 8.49 (brs, 1H) Mass: 394[M+H]⁺

Compound Ib-138

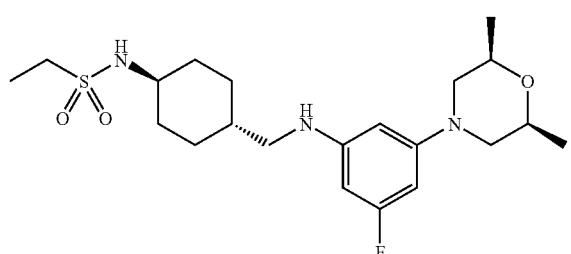
[Formula 169]



¹H-NMR (CDCl₃) δ: 1.02-1.34 (m, 4H), 1.37 (d, 6H, J=6.6 Hz), 1.57 (m, 1H), 1.87-1.97 (m, 2H), 2.07-2.18 (m, 2H), 2.93 (d, 2H, J=6.6 Hz), 3.13 (m, 1H), 3.25 (m, 1H), 3.99 (d, 1H, J=8.4 Hz), 6.38 (m, 1H), 6.49 (brs, 1H), 6.97 (q, 1H, J=9.3 Hz) Mass: 347[M+H]⁺

Compound II-2

[Formula 170]



¹H-NMR (DMSO-d₆) δ: 0.91-1.06 (m, 2H), 1.12-1.28 (m, 11H), 1.31-1.47 (m, 1H), 1.75-1.94 (m, 4H), 2.19 (t, 2H, J=11.3 Hz), 2.79 (t, 2H, J=6.0 Hz), 2.93-3.08 (m, 1H), 2.97 (q,

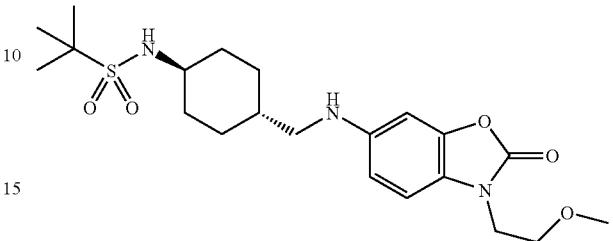
356

2H, J=7.42 Hz), 3.46 (m, 2H), 3.57-3.69 (m, 2H), 5.71 (t, 1H, J=5.2 Hz), 5.77 (d, 1H, J=11.5 Hz), 5.88-5.96 (m, 2H), 7.01 (d, 1H, J=7.4 Hz).

Compound II-3

5

[Formula 171]

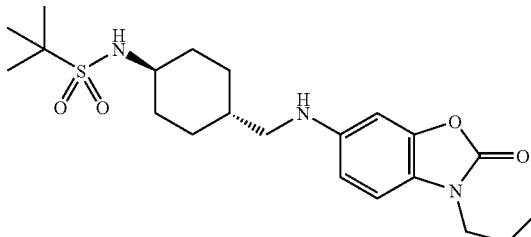


¹H-NMR (DMSO-d₆) δ: 0.90-1.07 (m, 2H), 1.15-1.21 (m, 1H), 1.27 (s, 9H), 1.40-1.49 (m, 2H), 1.82 (d, 2H, J=11.6 Hz), 1.92 (d, 2H, J=11.6 Hz), 2.79-2.84 (m, 2H), 2.97-3.10 (m, 1H), 3.24 (s, 3H), 3.55-3.62 (m, 2H), 3.84-3.91 (m, 2H), 5.50-5.59 (m, 1H), 6.40 (d, 1H, J=8.0 Hz), 6.56 (s, 1H), 6.72 (d, 1H, J=8.4 Hz), 6.97 (d, 1H, J=8.4 Hz). Melting point: 166 to 168°C.

Compound II-4

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[Formula 172]



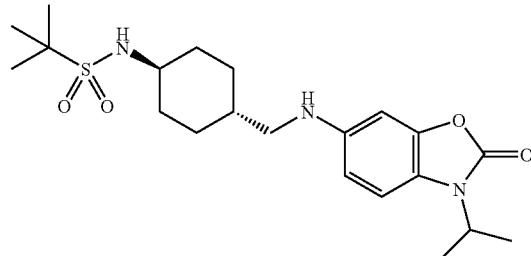
¹H-NMR (DMSO-d₆) δ: 0.87 (t, 3H, J=7.2 Hz), 0.93-1.06 (m, 2H), 1.13-1.21 (m, 1H), 1.26 (s, 9H), 1.37-1.49 (m, 2H), 1.61-1.72 (m, 2H), 1.82 (d, 2H, J=12.0 Hz), 1.91 (d, 2H, J=12.0 Hz), 2.78-2.84 (m, 2H), 2.97-3.08 (m, 1H), 3.61-3.71 (m, 2H), 5.52-5.60 (m, 1H), 6.40 (d, 1H, J=8.4 Hz), 6.56 (s, 1H), 6.73 (d, 1H, J=8.8 Hz), 6.97 (d, 1H, J=8.8 Hz).

Melting point: 185 to 186°C.

Compound II-5

45

[Formula 173]

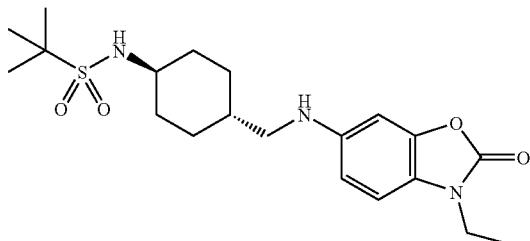


¹H-NMR (DMSO-d₆) δ: 0.90-1.05 (m, 2H), 1.26 (s, 9H), 1.28-1.31 (m, 1H), 1.35-1.47 (m, 8H), 1.81 (d, 2H, J=12.4 Hz), 1.91 (d, 2H, J=12.4 Hz), 2.77-2.84 (m, 2H), 2.96-3.07 (m, 1H), 4.30-4.42 (m, 1H), 5.51-5.64 (m, 1H), 6.39 (d, 1H,

357

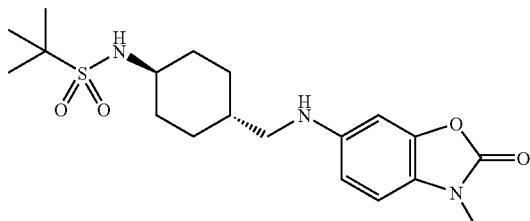
$J=8.0$ Hz), 6.55 (s, 1H), 6.72 (d, 1H, $J=8.8$ Hz), 7.07 (d, 1H, $J=8.8$ Hz). Melting point: 156 to 157° C.

Compound II-6



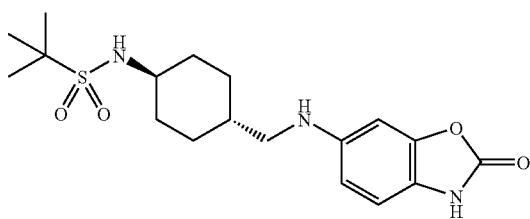
1H-NMR (DMSO-d₆) δ: 0.91-1.07 (m, 2H), 1.19-1.25 (m, 4H), 1.26 (s, 9H), 1.38-1.49 (m, 2H), 1.82 (d, 2H, $J=8.8$ Hz), 1.91 (d, 2H, $J=8.8$ Hz), 2.79-2.84 (m, 2H), 2.97-3.07 (m, 11H), 3.69-3.80 (m, 2H), 5.51-5.63 (m, 1H), 6.41 (d, 1H, $J=8.0$ Hz), 6.56 (s, 1H), 6.72 (d, 1H, $J=8.8$ Hz), 6.97 (d, 1H, $J=8.8$ Hz). Melting point: 178 to 179° C.

Compound II-7



1H-NMR (DMSO-d₆) δ: 0.92-1.07 (m, 2H), 1.19-1.22 (m, 1H), 1.26 (s, 9H), 1.38-1.48 (m, 2H), 1.82 (d, 2H, $J=11.6$ Hz), 1.91 (d, 2H, $J=11.6$ Hz), 2.79-2.84 (m, 2H), 2.95-3.09 (m, 1H), 3.25 (s, 3H), 5.52-5.60 (m, 1H), 6.41 (d, 1H, $J=8.4$ Hz), 6.56 (s, 1H), 6.72 (d, 1H, $J=8.4$ Hz), 6.92 (d, 1H, $J=8.4$ Hz). Melting point: 206 to 207° C.

Compound II-8

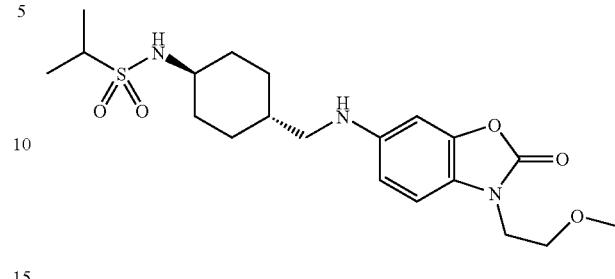


1H-NMR (DMSO-d₆) δ: 0.91-1.05 (m, 2H), 1.16-1.24 (m, 1H), 1.26 (s, 9H), 1.37-1.47 (m, 2H), 1.81 (d, 2H, $J=12.8$ Hz), 1.90 (d, 2H, $J=12.8$ Hz), 2.75-2.81 (m, 2H), 2.96-3.08 (m, 1H), 5.45-5.52 (m, 1H), 6.33 (d, 1H, $J=8.4$ Hz), 6.50 (s, 1H), 6.68-6.80 (m, 2H), 11.02 (brs, 1H). Melting point: 213 to 214° C.

358

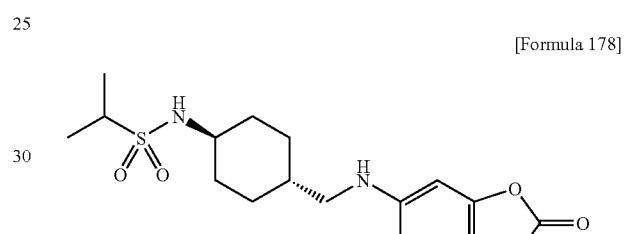
Compound II-9

[Formula 177]



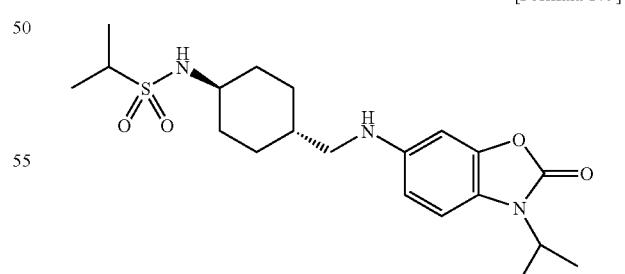
1H-NMR (DMSO-d₆) δ: 0.91-1.08 (m, 2H), 1.17-1.30 (m, 8H), 1.44 (brs, 1H), 1.82 (d, 2H, $J=12.4$ Hz), 1.89 (d, 2H, $J=12.4$ Hz), 2.78-2.82 (m, 2H), 2.97-3.15 (m, 2H), 3.23 (s, 3H), 3.55-3.62 (m, 2H), 3.83-3.90 (m, 2H), 5.52-5.59 (m, 1H), 6.40 (d, 1H, $J=8.0$ Hz), 6.55 (s, 1H), 6.92 (d, 1H, $J=8.0$ Hz), 6.97 (d, 1H, $J=8.4$ Hz). Melting point: 120 to 121° C.

Compound II-10



1H-NMR (DMSO-d₆) δ: 0.88 (t, 3H, $J=7.2$ Hz), 0.93-1.08 (m, 2H), 1.17-1.30 (m, 8H), 1.44 (brs, 1H), 1.52-1.61 (m, 2H), 1.83 (d, 2H, $J=12.0$ Hz), 1.90 (d, 2H, $J=12.0$ Hz), 2.78-2.84 (m, 2H), 2.98-3.15 (m, 2H), 3.62-3.71 (m, 2H), 5.52-5.60 (m, 1H), 6.41 (d, 1H, $J=8.4$ Hz), 6.57 (s, 1H), 6.92 (d, 1H, $J=8.0$ Hz), 6.97 (d, 1H, $J=8.4$ Hz). Melting point: 144 to 145° C.

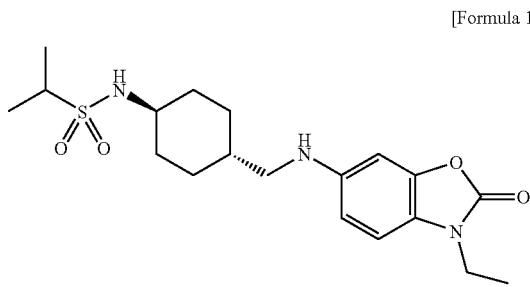
Compound II-11



1H-NMR (DMSO-d₆) δ: 0.90-1.08 (m, 2H), 1.15-1.30 (m, 8H), 1.33-1.50 (m, 7H), 1.82 (d, 2H, $J=12.0$ Hz), 1.89 (d, 2H, $J=12.0$ Hz), 2.78-2.86 (m, 2H), 2.96-3.14 (m, 2H), 4.30-4.45 (m, 1H), 5.50-5.61 (m, 1H), 6.40 (d, 1H, $J=7.6$ Hz), 6.55 (s, 1H), 6.92 (d, 1H, $J=7.2$ Hz), 7.07 (d, 1H, $J=7.6$ Hz). Melting point: 137 to 138° C.

359

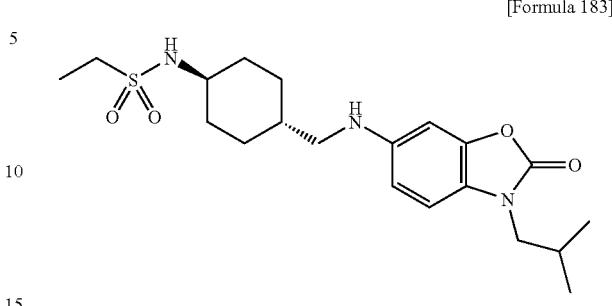
Compound II-12



[Formula 180]

1H-NMR (DMSO-d₆) δ: 0.92-1.07 (m, 2H), 1.14-1.30 (m, 1H), 1.36-1.50 (m, 1H), 1.82 (d, 2H, J=12.0 Hz), 1.89 (d, 2H, J=12.0 Hz), 2.78-2.85 (m, 2H), 2.97-3.15 (m, 2H), 3.69-3.79 (m, 2H), 5.52-5.60 (m, 1H), 6.41 (d, 1H, J=8.4 Hz), 6.56 (s, 1H), 6.92 (d, 1H, J=7.2 Hz), 6.98 (d, 1H, J=8.4 Hz). Melting point: 158 to 159° C.

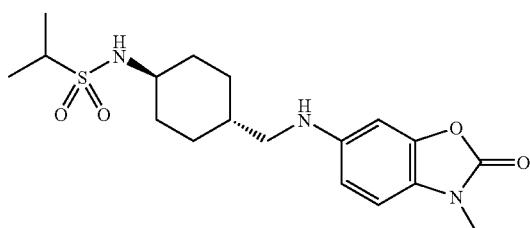
Compound II-13



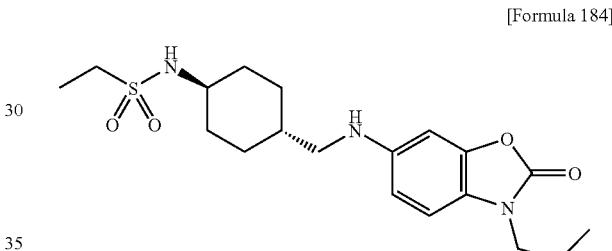
[Formula 183]

1H-NMR (DMSO-d₆) δ: 0.88 (s, 3H), 0.90 (s, 3H), 0.92-1.08 (m, 2H), 1.12-1.30 (m, 5H), 1.35-1.51 (m, 1H), 1.83 (d, 2H, J=12.4 Hz), 1.89 (d, 2H, J=12.4 Hz), 2.00-2.16 (m, 1H), 2.77-2.84 (m, 2H), 2.90-3.10 (m, 3H), 3.42-3.55 (m, 2H), 5.50-5.65 (m, 1H), 6.40 (d, 1H, J=8.4 Hz), 6.56 (s, 1H), 6.88-7.01 (m, 2H). Melting point: 132 to 133° C.

Compound II-16



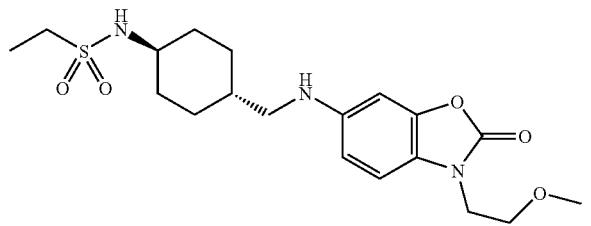
[Formula 181]



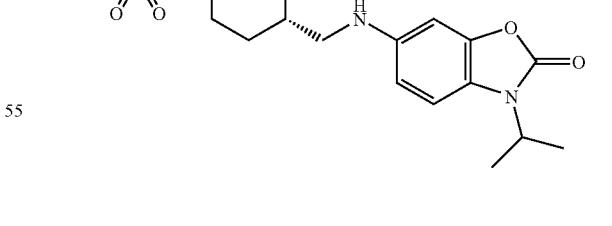
[Formula 184]

1H-NMR (DMSO-d₆) δ: 0.90-1.06 (m, 2H), 1.12-1.30 (m, 8H), 1.34-1.51 (m, 1H), 1.82 (d, 2H, J=12.0 Hz), 1.88 (d, 2H, J=12.0 Hz), 2.77-2.83 (m, 2H), 2.95-3.12 (m, 2H), 3.25 (s, 3H), 5.51-5.59 (m, 1H), 6.41 (d, 1H, J=8.8 Hz), 6.56 (s, 1H), 6.86-6.97 (m, 2H). Melting point: 157 to 158° C.

Compound II-14



[Formula 182]



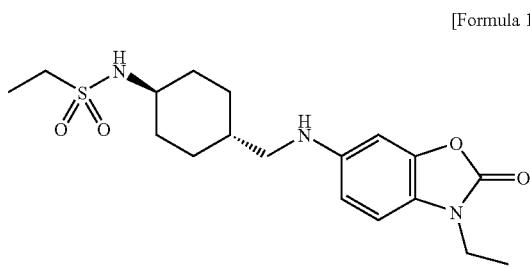
[Formula 185]

1H-NMR (DMSO-d₆) δ: 0.91-1.08 (m, 2H), 1.12-1.30 (m, 5H), 1.38-1.50 (m, 1H), 1.82 (d, 2H, J=12.0 Hz), 1.88 (d, 2H, J=12.0 Hz), 2.77-2.85 (m, 2H), 2.90-3.09 (m, 3H), 3.23 (s, 3H), 3.55-3.61 (m, 2H), 3.84-3.91 (m, 2H), 5.52-5.60 (m, 1H), 6.40 (d, 1H, J=8.4 Hz), 6.55 (s, 1H), 6.89-7.00 (m, 2H). Melting point: 150 to 151° C.

1H-NMR (DMSO-d₆) δ: 0.92-1.06 (m, 2H), 1.12-1.28 (m, 5H), 1.33-1.50 (m, 7H), 1.81 (d, 2H, J=12.0 Hz), 1.88 (d, 2H, J=12.0 Hz), 2.78-2.84 (m, 2H), 2.90-3.08 (m, 3H), 4.28-4.44 (m, 1H), 5.49-5.79 (m, 1H), 6.39 (d, 1H, J=8.0 Hz), 6.55 (s, 1H), 6.97 (d, 1H, J=7.6 Hz), 7.07 (d, 1H, J=8.0 Hz). Melting point: 124 to 125° C.

361

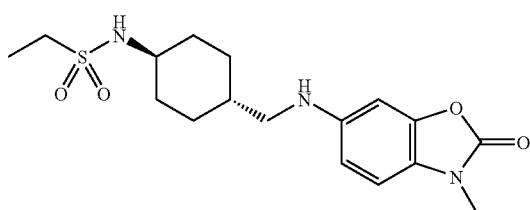
Compound II-18



¹H-NMR (DMSO-d₆) δ: 0.90-1.07 (m, 2H), 1.12-1.29 (m, 8H), 1.36-1.51 (m, 1H), 1.82 (d, 2H, J=12.0 Hz), 1.89 (d, 2H, J=12.0 Hz), 2.78-2.86 (m, 2H), 2.90-3.09 (m, 3H), 3.68-3.80 (m, 2H), 5.51-5.61 (m, 1H), 6.41 (d, 1H, J=8.4 Hz), 6.57 (s, 1H), 6.97 (d, 2H, J=8.4 Hz). Melting point: 163 to 164° C.

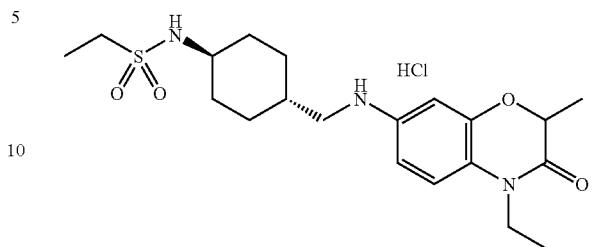
Compound II-19

[Formula 187]



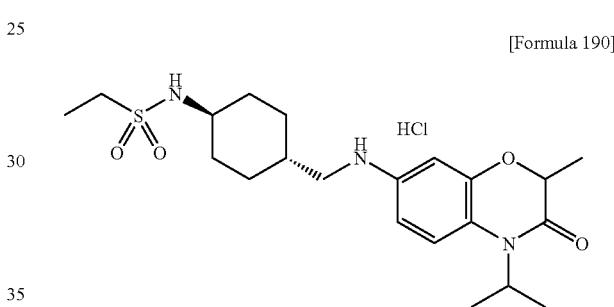
¹H-NMR (DMSO-d₆) δ: 0.89-1.08 (m, 2H), 1.11-1.30 (m, 5H), 1.35-1.51 (m, 1H), 1.82 (d, 2H, J=10.8 Hz), 1.89 (d, 2H, J=10.8 Hz), 2.75-2.88 (m, 2H), 2.89-3.10 (m, 3H), 3.25 (s, 3H), 5.48-5.60 (m, 1H), 6.42 (d, 1H, J=7.6 Hz), 6.56 (s, 1H), 6.92 (d, 1H, J=7.6 Hz), 6.98 (d, 1H, J=5.6 Hz). Melting point: 189 to 190° C.

Compound II-20



¹H-NMR (DMSO-d₆) δ: 0.86-1.25 (m, 10H), 1.40 (d, 3H, J=6.9 Hz), 1.52 (m, 1H), 1.82-1.93 (m, 4H), 2.95-3.00 (m, 5H), 3.63-3.91 (m, 2H), 4.61-4.68 (m, 1H), 6.73 (brs, 2H), 7.01 (d, 2H, J=7.8 Hz), 7.11 (d, 1H, J=8.1 Hz).

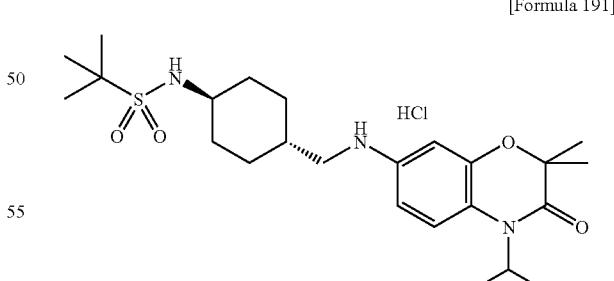
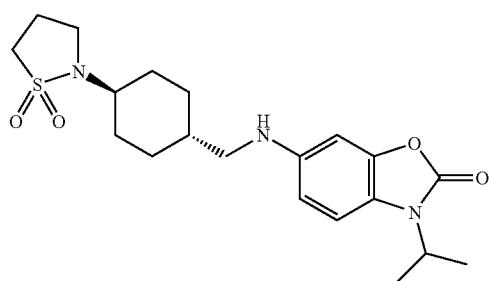
Compound II-22



¹H-NMR (DMSO-d₆) δ: 0.98-1.10 (m, 2H), 1.15-1.34 (m, 5H), 1.36-1.43 (m, 9H), 1.53 (m, 1H), 1.82-1.93 (m, 4H), 2.94-3.01 (m, 6H), 4.52 (m, 1H), 4.63 (m, 1H), 6.73 (brs, 2H), 7.02 (d, 1H, J=7.5 Hz), 7.21-7.25 (m, 1H).

Compound II-23

[Formula 188]



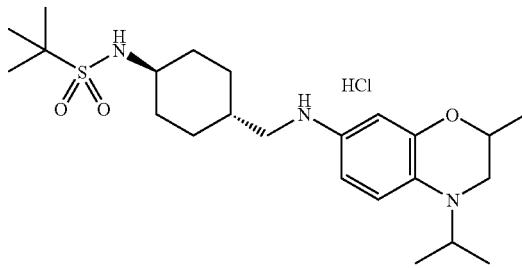
¹H-NMR (DMSO-d₆) δ: 0.86-1.04 (m, 4H), 1.25 (s, 10H), 1.30 (s, 6H), 1.38 (s, 3H), 1.40 (s, 3H), 178-1.92 (m 4H), 2.76-2.80 (m, 2H), 3.03 (m, 1H), 4.54-4.63 (m, 1H), 5.57 (m, 1H), 6.16 (s, 1H), 6.22 (d, 1H, J=8.4 Hz), 6.76 (d, 1H, J=8.4 Hz), 6.98 (d, 1H, J=8.4 Hz).

¹H-NMR (DMSO-d₆) δ: 0.95-1.13 (m, 2H), 1.31-1.59 (m, 10H), 1.73-1.92 (m, 4H), 2.12-2.26 (m, 2H), 2.84 (d, 2H, J=6.0 Hz), 3.07-3.30 (m, 4H), 4.30-4.46 (m, 1H), 5.64 (brs, 1H), 6.41 (d, 1H, J=8.4 Hz), 6.57 (s, 1H), 7.08 (d, 1H, J=8.4 Hz). Melting point: 165 to 166° C.

363

Compound II-24

[Formula 192]

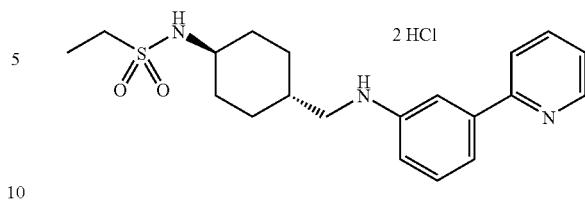


1H-NMR (DMSO-d₆) δ: 0.98-1.11 (m, 5H), 1.15-1.31 (m, 20H), 1.57 (m, 1H), 1.82-1.93 (m, 4H), 2.74-2.81 (m, 1H), 3.01-3.06 (m, 2H), 3.35 (m, 1H), 3.40 (m, 1H), 4.04-4.17 (m, 3H), 6.77 (d, 1H, $J=9.0$ Hz),

Compound II-25

Compound II-28

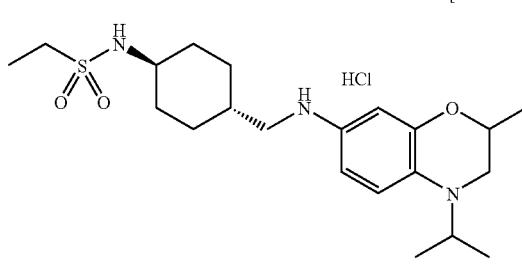
[Formula 196]



1H-NMR (DMSO-d₆) δ: 1.04-1.11 (m, 2H), 1.15-1.28 (m, 2H), 1.19 (t, 3H, $J=7.2$ Hz), 1.59 (m, 1H), 1.87-1.91 (m, 4H), 2.93-3.08 (m, 2H), 2.97 (q, 2H, $J=7.2$ Hz), 3.06-3.08 (m, 2H), 7.01 (m, 1H), 7.17 (d, 1H, $J=7.5$ Hz), 7.43 (d, 1H, $J=7.5$ Hz), 7.50-7.57 (m, 2H), 7.80-7.84 (m, 1H), 8.25-8.27 (m, 1H), 8.39-8.44 (m, 1H), 8.80-8.82 (m, 1H)

Compound II-29

[Formula 197]



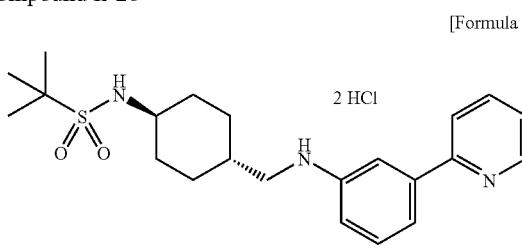
1H-NMR (DMSO-d₆) δ: 0.98-1.20 (m, 13H), 1.30 (d, 3H, $J=3$ Hz), 1.59 (m, 1H), 1.81-1.91 (m, 4H), 2.73-2.83 (m, 1H), 2.94-3.04 (m, 4H), 3.35-3.45 (m, 2H), 4.08-4.19 (m, 3H), 6.88 (brs, 3H), 7.03 (d, 1H, $J=8.4$ Hz).

Compound II-26

1H-NMR (DMSO-d₆) δ: 0.99-1.10 (m, 2H), 1.15-1.28 (m, 2H), 1.19 (t, 3H, $J=7.5$ Hz), 1.52 (m, 1H), 1.84-1.91 (m, 4H), 2.94-3.01 (m, 5H), 6.88 (m, 1H), 7.00 (d, 1H, $J=7.8$ Hz), 7.26-7.28 (m, 2H), 7.38 (m, 1H), 7.76 (d, 1H, $J=3.3$ Hz), 7.90 (d, 1H, $J=3.3$ Hz)

Compound II-30

[Formula 198]



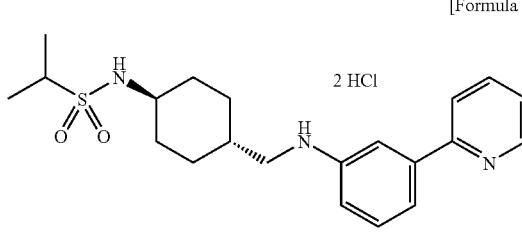
1H-NMR (DMSO-d₆) δ: 1.02-1.10 (m, 2H), 1.19-1.32 (m, 2H), 1.26 (s, 9H), 1.55 (m, 1H), 1.86-1.93 (m, 4H), 3.01-3.04 (m, 3H), 6.76 (d, 1H, $J=8.7$ Hz), 7.03 (m, 1H), 7.37-7.43 (m, 3H), 7.76-7.80 (m, 1H), 8.20-8.23 (m, 1H), 8.34-8.40 (m, 1H), 8.78-8.79 (m, 1H)

Compound II-27

1H-NMR (DMSO-d₆) δ: 0.93-1.08 (m, 2H), 1.18-1.33 (m, 2H), 1.26 (s, 9H), 1.45 (m, 1H), 1.78-1.97 (m, 4H), 2.86-2.94 (m, 2H), 2.95-3.10 (m, 11H), 5.91 (m, 1H), 6.55 (d, 1H, $J=7.6$ Hz), 6.63-6.71 (m, 2H), 6.73 (d, 1H, $J=8.0$ Hz), 7.06 (s, 1H), 7.15 (t, 1H, $J=8.0$ Hz), 7.60 (s, 1H), 8.11 (s, 11H), 8.31 (s, 1H)

Compound II-31

[Formula 199]

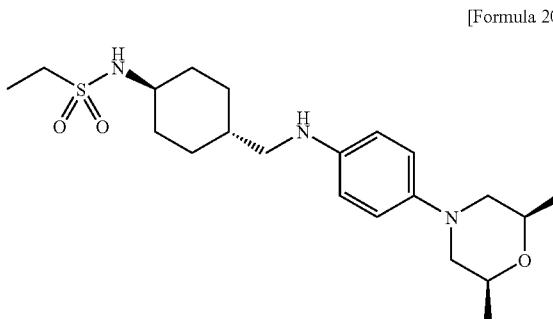


1H-NMR (DMSO-d₆) δ: 1.03-1.10 (m, 2H), 1.20-1.30 (m, 2H), 1.21 (d, 6H, $J=6.9$ Hz), 1.53 (m, 1H), 1.88 (m, 4H), 2.99-3.15 (m, 3H), 7.33-7.35 (m, 3H), 7.71-7.75 (m, 1H), 8.16-8.18 (m, 1H), 8.29-8.32 (m, 1H), 8.76-8.78 (m, 1H)

1H-NMR (DMSO-d₆) δ: 0.93-1.08 (m, 2H), 1.13-1.28 (m, 2H), 1.26 (s, 9H), 1.43 (m, 1H), 1.76-1.97 (m, 4H), 2.83-3.18 (m, 3H), 5.79 (m, 1H), 6.21 (s, 2H), 6.44 (d, 1H, $J=6.8$ Hz), 6.58-6.67 (m, 2H), 6.73 (d, 1H, $J=8.0$ Hz), 7.10 (t, 1H, $J=8.0$ Hz), 7.21 (s, 2H) Melting point: 205 to 206 °C.

365

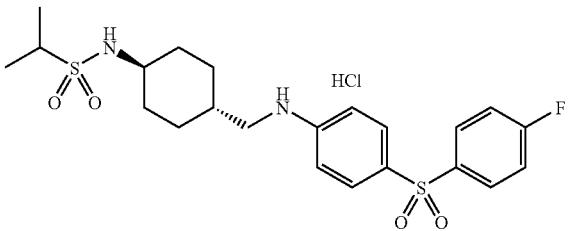
Compound II-32



¹H-NMR (DMSO-d₆) δ: 0.90-1.05 (m, 2H), 1.05-1.28 (m, 1H), 1.41 (m, 1H), 1.75-1.92 (m, 4H), 2.11 (t, 2H, J=10.0 Hz), 2.73-2.82 (m, 2H), 2.91-3.08 (m, 3H), 3.24 (d, 2H, J=11.2 Hz), 3.62-3.72 (m, 2H), 5.07 (m, 1H), 6.47 (d, 2H, J=7.2 Hz), 6.72 (d, 2H, J=7.2 Hz), 6.97 (d, 1H, J=7.6 Hz)

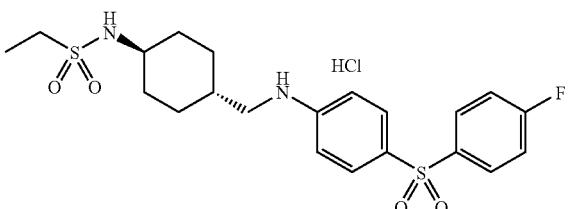
Melting point: 165 to 166°C.

Compound II-33



¹H-NMR (DMSO-d₆) δ: 0.91-1.06 (m, 2H), 1.15-1.26 (m, 8H), 1.33-1.48 (m, 1H), 1.71-1.93 (m, 4H), 2.88 (d, 2H, J=6.5 Hz), 2.93-3.15 (m, 2H), 5.70 (brs, 2H), 6.63 (d, 2H, J=9.1 Hz), 6.93-6.96 (m, 1H), 7.38-7.42 (m, 2H), 7.57 (d, 2H, J=9.1 Hz), 7.88-7.93 (m, 2H)

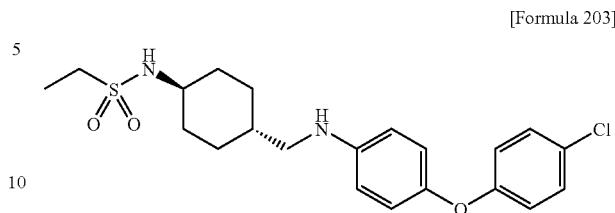
Compound II-34



¹H-NMR (DMSO-d₆) δ: 0.98-1.02 (m, 2H), 1.16-1.18 (m, 5H), 1.42 (s, 1H), 1.75-1.91 (m, 4H), 2.88 (d, 2H, J=6.6 Hz), 2.96 (q, 3H, J=7.3 Hz), 6.63 (d, 2H, J=8.9 Hz), 6.99-7.02 (m, 1H), 7.38-7.41 (m, 2H), 7.57 (d, 2H, J=8.9 Hz), 7.89-7.92 (m, 2H).

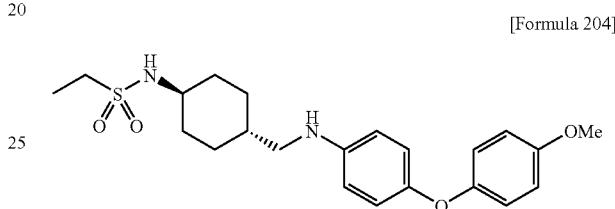
366

Compound II-35



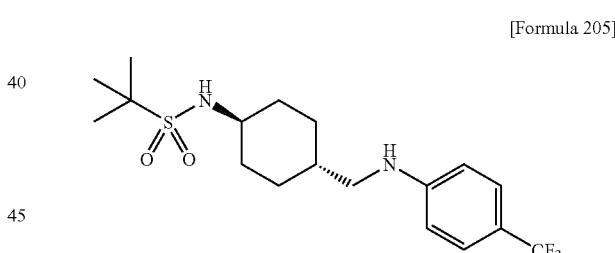
¹H-NMR (DMSO-d₆) δ: 0.90-1.52 (m, 5H), 1.19 (t, 3H, J=7.2 Hz), 1.75-1.96 (m, 4H), 2.50-3.10 (m, 3H), 2.62 (q, 2H, J=7.2 Hz), 5.55-5.70 (m, 1H), 6.57 (d, 2H, J=8.7 Hz), 6.80-7.04 (m, 4H), 7.01 (d, 1H, J=7.8 Hz), 7.34 (d, 2H, J=8.7 Hz)

Compound II-36



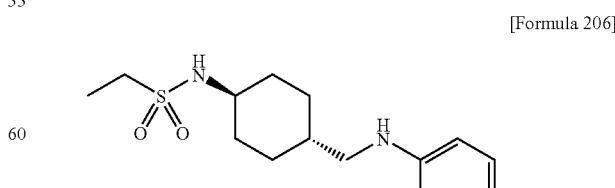
¹H-NMR (DMSO-d₆) δ: 0.90-1.50 (m, 5H), 1.19 (t, 3H, J=7.2 Hz), 1.75-1.95 (m, 4H), 2.70-3.10 (m, 3H), 2.97 (q, 2H, J=7.2 Hz), 3.70 (s, 3H), 5.40-5.50 (m, 1H), 6.53 (d, 2H, J=8.7 Hz), 6.74 (d, 2H, J=8.7 Hz), 6.78-6.90 (m, 4H), 6.99 (d, 1H, J=7.8 Hz)

Compound II-37



¹H-NMR (CDCl₃) δ: 1.02-1.32 (m, 4H), 1.39 (s, 9H), 1.58 (m, 1H), 1.86-1.96 (m, 2H), 2.12-2.22 (m, 2H), 3.02 (d, 2H, J=6.6 Hz), 3.25 (m, 1H), 3.67 (d, 1H, J=9.3 Hz), 6.67 (d, 2H, J=8.7 Hz), 7.41 (d, 2H, J=8.7 Hz) Mass: 393[M+H]

Compound II-38



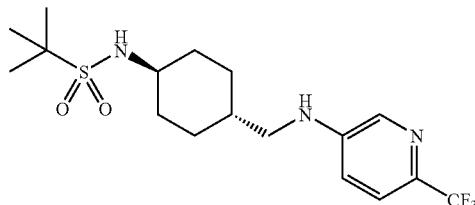
¹H-NMR (DMSO-d₆) δ: 0.93-1.07 (m, 2H), 1.17-1.26 (m, 2H), 1.19 (t, 3H, J=7.1 Hz), 1.43 (s, 1H), 1.77-1.85 (m, 2H),

367

1.85-1.94 (m, 2H), 2.82 (t, 1H, $J=5.8$ Hz), 2.98 (m, 1H), 2.97 (q, 2H, $J=7.1$ Hz), 5.87 (m, 1H), 6.56 (d, 2H, $J=8.6$ Hz), 6.98 (d, 1H, $J=7.6$ Hz), 7.02 (d, 2H, $J=8.6$ Hz).

Compound II-39

[Formula 207]



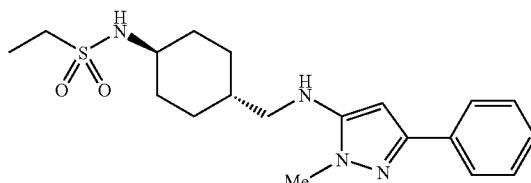
5

368

Hz), 3.02 (m, 1H), 3.71 (s, 3H), 5.26 (m, 1H), 6.58 (d, 1H, $J=8.6$ Hz), 6.98 (d, 2H, $J=7.8$ Hz), 7.02 (d, 2H, $J=8.6$ Hz), 7.44 (br s, 1H).

Compound II-43

[Formula 211]

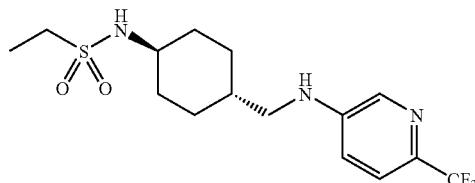


15

¹H-NMR (DMSO-d₆) δ: 0.98-1.10 (m, 2H), 1.19-1.35 (m, 2H), 1.29 (s, 9H), 1.46 (s, 1H), 1.73-1.98 (m, 4H), 2.93 (m, 1H), 3.04 (m, 1H), 6.60-6.69 (m, 2H), 6.75 (d, 1H, $J=8.8$ Hz), 6.97 (d, 1H, $J=7.6$ Hz), 7.49 (d, 1H, $J=8.8$ Hz), 8.05 (s, 1H).

Compound II-40

[Formula 208]

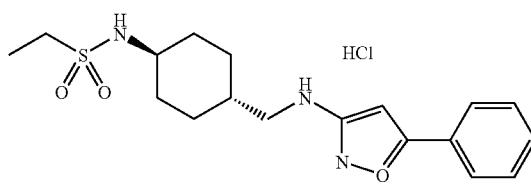


20

¹H-NMR (DMSO-d₆) δ: 0.98-1.06 (m, 2H), 1.16-1.25 (m, 2H), 1.18 (t, 3H, $J=7.5$ Hz), 1.51 (m, 1H), 1.83-1.91 (m, 4H), 2.85 (t, 2H, $J=6.3$ Hz), 2.97 (q, 2H, $J=7.5$ Hz), 3.04 (m, 1H), 3.56 (s, 3H), 5.46 (t, 1H, $J=6.3$ Hz), 5.76 (s, 1H), 6.49 (d, 1H, $J=7.8$ Hz), 7.21 (t, 1H, $J=7.5$ Hz), 7.32 (t, 2H, $J=7.5$ Hz), 7.68 (d, 2H, $J=7.5$ Hz)

Compound II-44

[Formula 212]

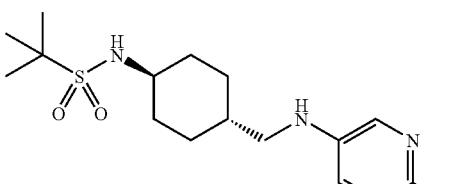


25

¹H-NMR (DMSO-d₆) δ: 0.96-1.09 (m, 2H), 1.16-1.29 (m, 2H), 1.19 (t, 3H, $J=7.3$ Hz), 1.45 (s, 1H), 1.76-1.94 (m, 4H), 1.76 (s, 2H), 2.93 (t, 2H, $J=5.8$ Hz), 2.97 (q, 2H, $J=7.3$ Hz), 6.66 (s, 1H), 6.94-7.01 (m, 2H), 7.49 (d, 1H, $J=8.6$ Hz), 8.04 (s, 1H).

Compound II-41

[Formula 209]

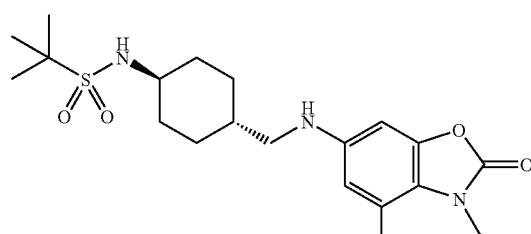


30

¹H-NMR (DMSO-d₆) δ: 0.96-1.05 (m, 2H), 1.18 (t, 3H, $J=7.2$ Hz), 1.24 (m, 2H), 1.48 (m, 1H), 1.76-1.91 (m, 4H), 2.91 (d, 2H, $J=6.6$ Hz), 2.97 (q, 2H, $J=7.2$ Hz), 6.35 (s, 1H), 6.99 (d, 1H, $J=7.8$ Hz), 7.46-7.49 (m, 3H), 7.73-7.76 (m, 2H)

Compound II-45

[Formula 213]



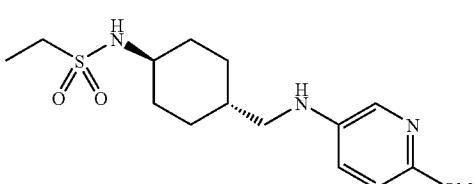
35

¹H-NMR (DMSO-d₆) δ: 0.91-1.05 (m, 2H), 1.17-1.33 (m, 2H), 1.26 (s, 9H), 1.35-1.48 (m, 1H), 1.76-1.86 (m, 2H), 1.86-1.95 (m, 2H), 2.76-2.82 (m, 1H), 2.96-3.08 (m, 1H), 3.71 (s, 3H), 5.21-5.30 (m, 1H), 6.57 (d, 1H, $J=8.6$ Hz), 6.73 (d, 1H, $J=8.6$ Hz), 7.02 (dd, 1H, $J=8.6, 2.3$ Hz), 7.44 (d, 1H, $J=2.3$ Hz).

Compound II-42

[Formula 210]

45



55

¹H-NMR (DMSO-d₆) δ: 0.92-1.08 (m, 2H), 1.15-1.22 (m, 1H), 1.26 (s, 9H), 1.37-1.51 (m, 2H), 1.81 (d, 2H, $J=11.6$ Hz), 1.91 (d, 2H, $J=11.6$ Hz), 2.76-2.86 (m, 2H), 2.97-3.08 (m, 1H), 3.35 (s, 3H), 5.82-5.91 (m, 1H), 6.26 (d, 1H, $J=13.6$ Hz), 6.39 (s, 1H), 6.73 (brs, 1H).

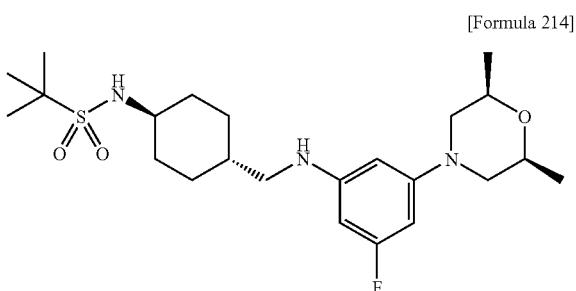
Melting point: 215 to 216°C.

¹H-NMR (DMSO-d₆) δ: 0.98-1.01 (m, 2H), 1.18-1.28 (m, 2H), 1.19 (t, 3H, $J=7.1$ Hz), 1.42 (s, 1H), 1.76-1.85 (m, 2H), 1.85-1.93 (m, 2H), 2.79 (t, 2H, $J=5.9$ Hz), 2.97 (q, 2H, $J=7.1$

65

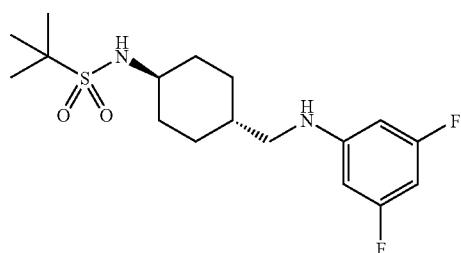
369

Compound II-46



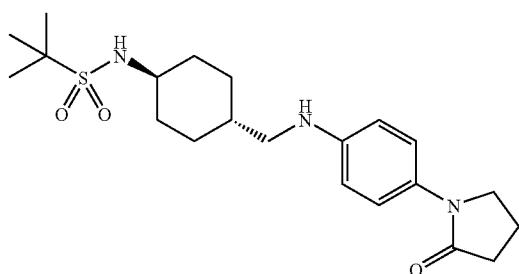
1H-NMR (CDCl₃) δ: 1.02-1.32 (m, 4H), 1.24 (d, 6H, J=6.0 Hz), 1.39 (s, 9H), 1.54 (m, 1H), 1.84-1.94 (m, 2H), 2.12-2.22 (m, 2H), 2.39 (t, 2H, J=10.5 Hz), 2.94 (d, 2H, J=6.9 Hz), 3.24 (m, 1H), 3.38 (d, 1H, J=9.6 Hz), 3.61 (d, 1H, J=9.6 Hz), 3.72-4.00 (m, 2H), 5.83-5.94 (m, 1H), 5.96-6.10 (m, 2H).

Compound II-47



1H-NMR (DMSO-d₆) δ: 0.91-1.07 (m, 2H), 1.16-1.34 (m, 11H), 1.40 (m, 1H), 1.79 (d, 2H, J=12.5 Hz), 1.90 (d, 2H, J=11.9 Hz), 2.82 (t, 2H, J=5.5 Hz), 3.01 (m, 1H), 6.12-6.18 (m, 3H), 6.30 (t, 1H, J=5.5 Hz), 6.76 (d, 1H, J=8.7 Hz).

Compound II-48

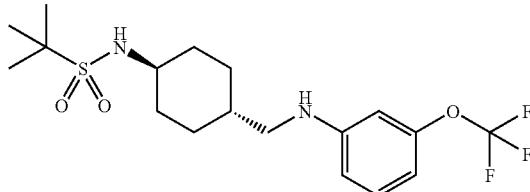


1H-NMR (CDCl₃) δ: 1.00-1.28 (m, 4H), 1.39 (s, 9H), 1.56 (m, 1H), 1.91 (d, 2H, J=12.4 Hz), 2.08-2.21 (m, 4H), 2.58 (t, 2H, J=8.1 Hz), 2.97 (d, 2H, J=6.0 Hz), 3.23 (m, 1H), 3.70 (d, 1H, J=9.4 Hz), 3.80 (t, 2H, J=7.1 Hz), 6.66 (d, 2H, J=8.7 Hz), 7.36 (d, 2H, J=8.7 Hz).

370

Compound II-49

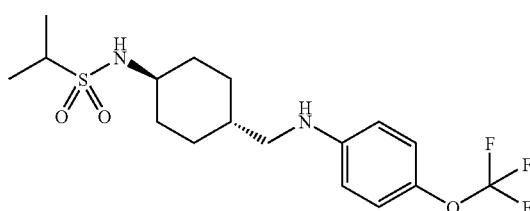
[Formula 217]



1H-NMR (DMSO-d₆) δ: 0.92-1.06 (m, 2H), 1.17-1.33 (m, 11H), 1.41 (m, 1H), 1.80 (d, 2H, J=12.9 Hz), 1.90 (d, 2H, J=11.4 Hz), 2.82 (t, 2H, J=6.1 Hz), 3.01 (m, 1H), 6.07 (t, 1H, J=5.3 Hz), 6.34-6.43 (m, 2H), 6.51 (dd, 1H, J₁=8.2 Hz, J₂=1.8 Hz), 6.75 (d, 1H, J=8.5 Hz), 7.11 (t, 1H, 8.2 Hz).

Compound II-50

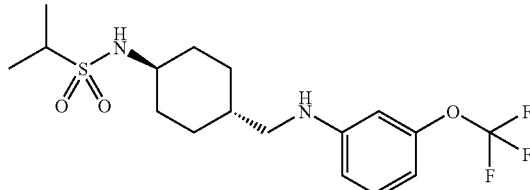
[Formula 218]



1H-NMR (DMSO-d₆) δ: 0.92-1.08 (m, 2H), 1.14-1.31 (m, 8H), 1.43 (m, 1H), 1.76-1.94 (m, 4H), 2.82 (t, 2H, J=6.0 Hz), 2.95-3.16 (m, 2H), 5.90 (t, 1H, J=5.5 Hz), 6.56 (d, 2H, J=8.7 Hz), 6.95 (d, 1H, J=7.9 Hz), 7.03 (d, 2H, J=8.6 Hz).

Compound II-51

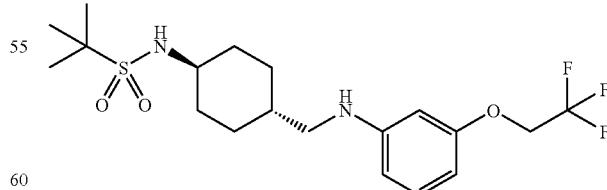
[Formula 219]



1H-NMR (DMSO-d₆) δ: 0.90-1.08 (m, 2H), 1.13-1.31 (m, 8H), 1.42 (m, 1H), 1.76-1.94 (m, 4H), 2.83 (t, 2H, J=6.0 Hz), 2.95-3.16 (m, 2H), 6.07 (t, 1H, J=5.4 Hz), 6.36-6.46 (m, 2H), 6.53 (dd, 1H, J₁=8.1 Hz, J₂=1.9 Hz), 6.95 (d, 1H, J=7.9 Hz), 7.12 (d, 1H, J=8.1 Hz).

Compound II-52

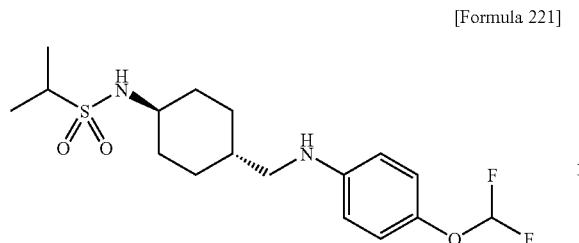
[Formula 220]



1H-NMR (DMSO-d₆) δ: 0.91-1.10 (m, 2H), 1.19-1.37 (m, 11H), 1.45 (m, 1H), 1.78-1.90 (m, 4H), 2.84 (t, 2H, J=6.0 Hz), 3.04 (m, 1H), 4.64 (q, 2H, J=9.0 Hz), 5.73 (t, 1H, J=5.4 Hz), 6.13-6.21 (m, 2H), 6.26 (d, 1H, J=7.2 Hz), 6.78 (d, 1H, J=8.4 Hz), 6.99 (t, 1H, 8.0 Hz).

371

Compound II-53

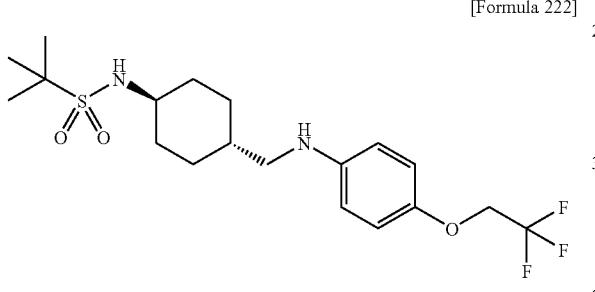


¹H-NMR (DMSO-d₆) δ: 0.90-1.06 (m, 2H), 1.13-1.30 (m, 8H), 1.42 (m, 1H), 1.75-1.93 (m, 4H), 2.80 (t, 2H, J=6.2 Hz), 2.93-3.16 (m, 2H), 5.66 (t, 1H, J=5.5 Hz), 6.53 (d, 2H, J=9.1 Hz), 6.89 (d, 2H, J=8.8 Hz), 6.92 (t, 1H, JH-F=75 Hz), 6.94 (d, 1H, J=8.0 Hz).

Compound II-54

¹H-NMR (DMSO-d₆) δ: 0.98-1.14 (m, 2H), 1.15-1.32 (m, 5H), 1.54 (m, 1H), 1.83-1.96 (m, 4H), 2.89-3.10 (m, 5H), 6.17 (t, 1H, J=5.2 Hz), 6.63 (d, 1H, J=2.2 Hz), 7.02 (d, 1H, J=7.7 Hz), 7.21 (dd, 1H, J₁=9.1 Hz, J₂=2.5 Hz), 7.27 (dd, 1H, J₁=8.2 Hz, J₂=4.4 Hz), 7.67 (d, 1H, J=9.1 Hz), 7.97 (d, 1H, J=8.2 Hz), 8.45 (dd, 1H, J₁=4.3 Hz, J₂=1.5 Hz).

Compound II-57

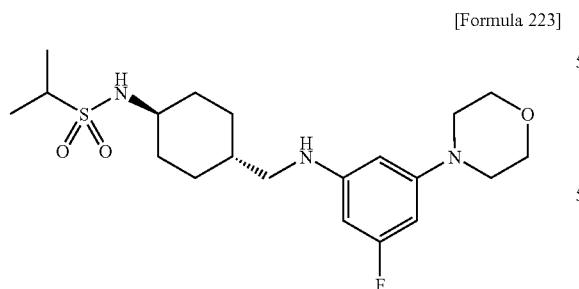


¹H-NMR (DMSO-d₆) δ: 0.88-1.05 (m, 2H), 1.14-1.32 (m, 11H), 1.41 (m, 1H), 1.75-1.94 (m, 4H), 2.77 (t, 2H, J=6.0 Hz), 3.01 (m, 1H), 4.54 (q, 2H, J=9.0 Hz), 5.33 (t, 1H, J=5.8 Hz), 6.49 (d, 2H, J=8.8 Hz), 6.75 (d, 1H, J=8.8 Hz), 6.80 (d, 2H, J=8.8 Hz).

Compound II-55

¹H-NMR (DMSO-d₆) δ: 0.97-1.14 (m, 2H), 1.17-1.34 (m, 8H), 1.54 (m, 1H), 1.83-1.96 (m, 4H), 2.94 (t, 2H, J=6.0 Hz), 2.99-3.18 (m, 2H), 6.17 (t, 1H, J=5.4 Hz), 6.63 (d, 1H, J=2.5 Hz), 6.96 (d, 1H, J=7.7 Hz), 7.21 (dd, 1H, J₁=9.1 Hz, J₂=2.5 Hz), 7.27 (dd, 1H, J₁=8.2 Hz, J₂=4.1 Hz), 7.67 (d, 1H, J=9.1 Hz), 7.97 (d, 1H, J=8.0 Hz), 8.45 (dd, 1H, J₁=4.3 Hz, J₂=1.5 Hz).

Compound II-58

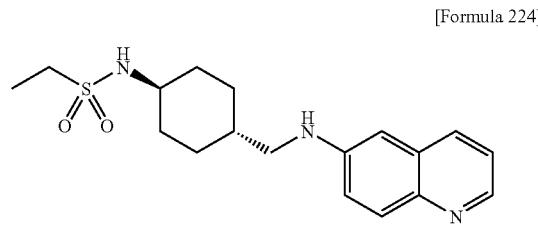


¹H-NMR (DMSO-d₆) δ: 0.90-1.06 (m, 2H), 1.14-1.31 (m, 8H), 1.40 (m, 1H), 1.74-1.93 (m, 4H), 2.79 (t, 2H, J=5.9 Hz), 2.94-3.15 (m, 6H), 3.69 (t, 4H, J=4.8 Hz), 5.70-5.94 (m, 4H), 6.94 (d, 1H, J=8.0 Hz).

¹H-NMR (DMSO-d₆) δ: 0.90-1.07 (m, 2H), 1.12-1.29 (m, 5H), 1.40 (m, 1H), 1.74-1.93 (m, 4H), 2.80 (t, 2H, J=5.9 Hz), 2.92-3.07 (m, 7H), 3.69 (t, 4H, J=4.8 Hz), 5.69-5.95 (m, 4H), 6.99 (d, 1H, J=7.7 Hz).

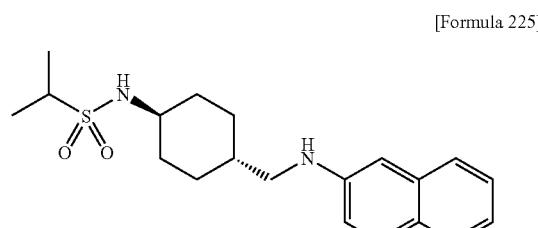
372

Compound II-56



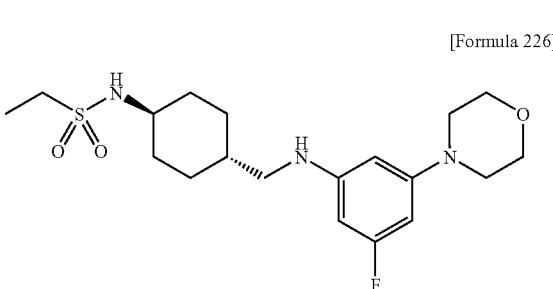
¹H-NMR (DMSO-d₆) δ: 0.98-1.14 (m, 2H), 1.15-1.32 (m, 5H), 1.54 (m, 1H), 1.83-1.96 (m, 4H), 2.89-3.10 (m, 5H), 6.17 (t, 1H, J=5.2 Hz), 6.63 (d, 1H, J=2.2 Hz), 7.02 (d, 1H, J=7.7 Hz), 7.21 (dd, 1H, J₁=9.1 Hz, J₂=2.5 Hz), 7.27 (dd, 1H, J₁=8.2 Hz, J₂=4.4 Hz), 7.67 (d, 1H, J=9.1 Hz), 7.97 (d, 1H, J=8.2 Hz), 8.45 (dd, 1H, J₁=4.3 Hz, J₂=1.5 Hz).

Compound II-57



¹H-NMR (DMSO-d₆) δ: 0.97-1.14 (m, 2H), 1.17-1.34 (m, 8H), 1.54 (m, 1H), 1.83-1.96 (m, 4H), 2.94 (t, 2H, J=6.0 Hz), 2.99-3.18 (m, 2H), 6.17 (t, 1H, J=5.4 Hz), 6.63 (d, 1H, J=2.5 Hz), 6.96 (d, 1H, J=7.7 Hz), 7.21 (dd, 1H, J₁=9.1 Hz, J₂=2.5 Hz), 7.27 (dd, 1H, J₁=8.2 Hz, J₂=4.1 Hz), 7.67 (d, 1H, J=9.1 Hz), 7.97 (d, 1H, J=8.0 Hz), 8.45 (dd, 1H, J₁=4.3 Hz, J₂=1.5 Hz).

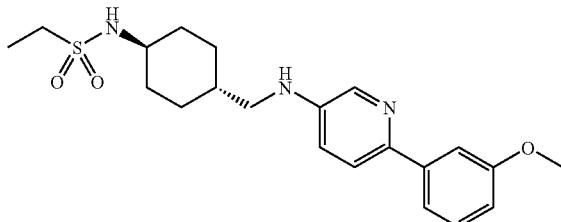
Compound II-58



373

Compound II-59

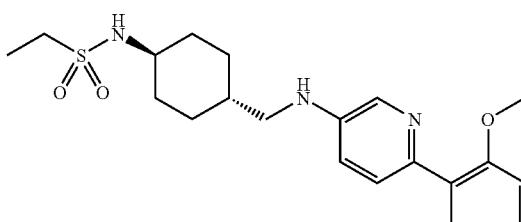
[Formula 227]



1H-NMR (DMSO-d₆) δ: 0.94-1.11 (m, 2H), 1.14-1.30 (m, 5H), 1.47 (m, 1H), 1.78-1.95 (m, 4H), 2.88-3.09 (m, 5H), 3.80 (s, 3H), 6.09 (t, 1H, J=5.6 Hz), 6.81-6.86 (m, 1H), 6.96 (dd, 1H, J₁=8.8 Hz, J₂=2.8 Hz), 7.01 (d, 1H, J=7.4 Hz), 7.29 (t, 1H, J=8.0 Hz), 7.45-7.51 (m, 2H), 7.66 (d, 1H, J=8.5 Hz), 8.04 (d, 1H, J=2.8 Hz).

Compound II-60

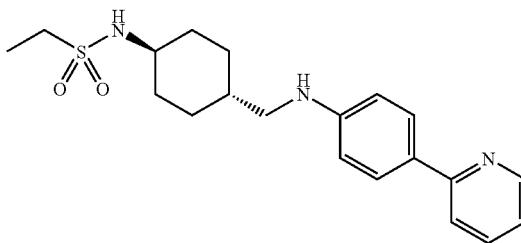
[Formula 228]



1H-NMR (DMSO-d₆) δ: 1.03 (m, 2H), 1.19 (t, 2H, J=7.8 Hz), 1.21 (m, 2H), 1.46 (m, 1H), 1.76-1.95 (m, 4H), 2.90 (t, 2H, J=5.8 Hz), 2.97 (q, 2H, J=7.3 Hz), 3.03 (m, 1H), 3.80 (s, 3H), 5.95 (m, 1H), 6.90 (m, 1H), 6.98 (d, 1H, J=7.8 Hz), 6.98 (dd, 1H, J=7.8, 7.8 Hz), 7.06 (d, 1H, J=8.6 Hz), 7.26 (dd, 1H, J=7.8, 7.8 Hz), 7.61 (d, 1H, J=8.6 Hz), 7.69 (d, 1H, J=7.8 Hz), 8.03 (s, 1H).

Compound II-61

[Formula 229]



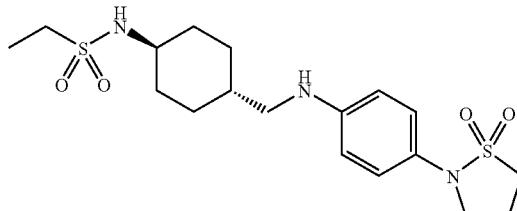
1H-NMR (DMSO-d₆) δ: 0.96-1.09 (m, 2H), 1.18-1.29 (m, 2H), 1.19 (t, 3H, J=7.6 Hz), 1.47 (m, 1H), 1.87 (m, 5H), 2.90 (t, 2H, J=6.3 Hz), 2.97 (q, 2H, J=7.6 Hz), 3.02 (m, 1H), 5.98

374

(m, 1H), 6.63 (d, 2H, J=8.3 Hz), 6.98 (d, 1H, J=7.3 Hz), 7.14 (m, 1H), 7.73 (s, 2H), 7.83 (d, 2H, J=8.3 Hz), 8.52 (d, 1H, J=4.0 Hz).

Compound II-62

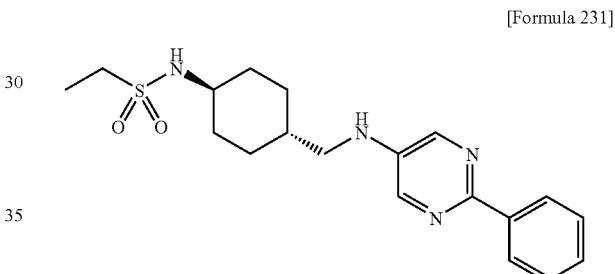
[Formula 230]



1H-NMR (DMSO-d₆) δ: 0.98-1.01 (m, 2H), 1.20 (s, 9H), 1.20-1.37 (m, 2H), 1.42 (m, 1H), 1.76-1.96 (m, 4H), 2.28-2.37 (m, 2H), 2.75-2.85 (m, 2H), 3.02 (m, 1H), 3.36 (t, 2H, J=7.8 Hz), 3.57 (t, 2H, J=6.3 Hz), 5.66 (m, 1H), 6.54 (d, 2H, J=8.0 Hz), 6.73 (d, 1H, J=8.6 Hz), 7.00 (d, 1H, J=8.0 Hz).

Compound II-63

25

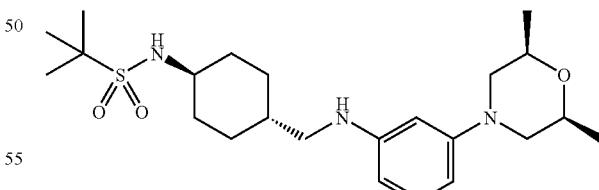


1H-NMR (DMSO-d₆) δ: 0.96-1.14 (m, 2H), 1.14-1.32 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.50 (m, 1H), 1.76-1.96 (m, 4H), 2.91-3.10 (m, 3H), 2.97 (q, 2H, J=7.2 Hz), 6.28 (m, 1H), 7.02 (d, 1H, J=7.8 Hz), 7.32-7.46 (m, 3H), 8.20 (d, 1H, J=6.9 Hz), 8.22 (s, 2H).

Compound II-64

45

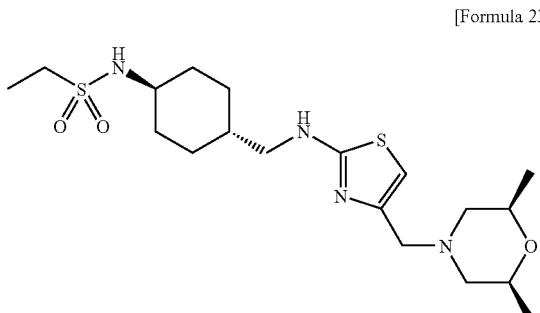
[Formula 231]



1H-NMR (DMSO-d₆) δ: 1.03-1.15 (m, 2H), 1.18-1.29 (m, 2H), 1.24 (d, 6H, J=6.3 Hz), 1.52 (m, 1H), 1.86-1.94 (m, 2H), 2.10-2.19 (m, 2H), 2.40 (t, 2H, J=6.0 Hz), 2.95 (d, 2H, J=6.0 Hz), 3.23 (m, 1H), 3.40 (d, 2H, J=11.4 Hz), 3.75-3.85 (m, 2H), 3.86 (d, 1H, J=9.3 Hz), 6.14 (d, 1H, J=8.5 Hz), 6.15 (s, 1H), 6.29 (d, 1H, J=8.5 Hz), 7.06 (d, 1H, J=8.5 Hz).

375

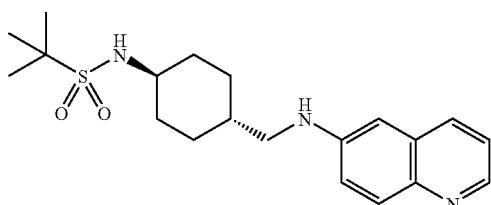
Compound II-65



[Formula 233]

¹H-NMR (CDCl₃) δ: 1.08-1.16 (m, 2H), 1.14 (d, 6H, J=6.8 Hz), 1.21-1.30 (m, 2H), 1.29 (s, 9H), 1.78 (t, 2H, J=10.6 Hz), 1.83-1.92 (m, 2H), 2.11-2.19 (m, 2H), 2.78 (d, 2H, J=10.6 Hz), 3.06 (s, 2H), 3.23 (m, 1H), 3.38 (s, 2H), 3.70-3.80 (m, 2H), 4.02 (d, 1H, J=9.9 Hz), 5.37 (s, 1H), 6.30 (s, 1H).

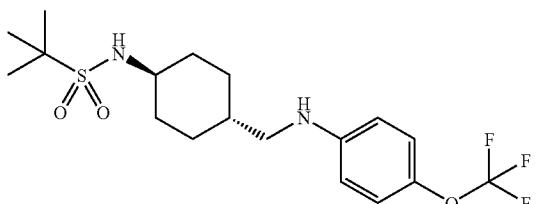
Compound II-66



[Formula 234]

¹H-NMR (DMSO-d₆) δ: 1.01-1.12 (m, 2H), 1.20-1.34 (m, 2H), 1.27 (s, 9H), 1.54 (m, 1H), 1.82-1.99 (m, 4H), 2.91-2.98 (m, 2H), 3.06 (m, 1H), 6.17 (s, 1H), 6.63 (d, 1H), 6.78 (d, 1H, J=9.0 Hz), 7.20 (m, 1H), 7.27 (m, 1H), 7.77 (d, 1H, J=9.0 Hz), 7.98 (d, 1H, J=9.0 Hz), 8.54 (s, 1H).

Compound II-67

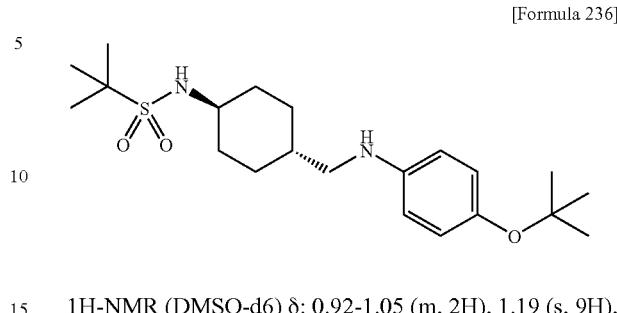


[Formula 235]

¹H-NMR (DMSO-d₆) δ: 0.92-1.06 (m, 2H), 1.20-1.32 (m, 2H), 1.26 (s, 9H), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 1.88-1.96 (m, 2H), 2.78-2.86 (m, 2H), 3.02 (m, 1H), 5.89 (s, 1H), 6.56 (d, 1H, J=8.4 Hz), 6.76 (d, 1H, J=8.4 Hz), 7.02 (d, 1H, J=8.4 Hz).

376

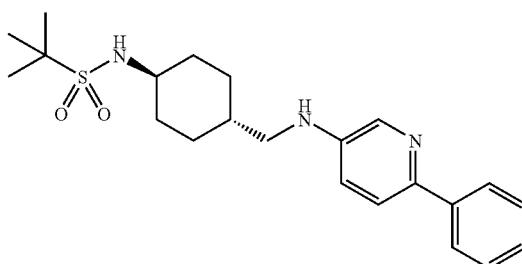
Compound II-68



[Formula 236]

¹H-NMR (DMSO-d₆) δ: 0.92-1.05 (m, 2H), 1.19 (s, 9H), 1.20-1.32 (m, 2H), 1.26 (s, 9H), 1.42 (m, 1H), 1.80-1.96 (m, 4H), 2.77 (s, 2H), 3.04 (m, 1H), 5.29 (s, 1H), 6.44 (d, 1H, J=7.2 Hz), 6.68 (d, 1H, J=7.2 Hz), 6.75 (d, 1H, J=8.4 Hz).

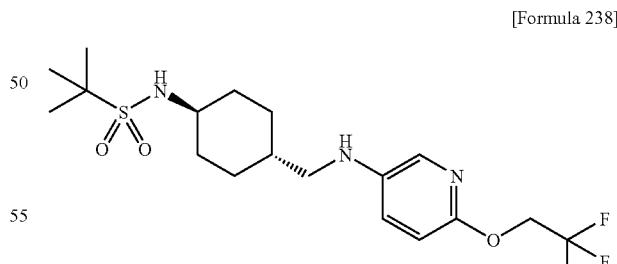
Compound II-69



[Formula 237]

¹H-NMR (DMSO-d₆) δ: 0.95-1.10 (m, 2H), 1.20-1.32 (m, 2H), 1.26 (s, 9H), 1.47 (m, 1H), 1.80-1.88 (m, 2H), 1.88-1.95 (m, 2H), 2.88-2.95 (m, 2H), 3.02 (s, 1H), 6.07 (m, 1H), 6.77 (d, 1H, J=8.4 Hz), 6.97 (d, 1H, J=7.6 Hz), 7.26 (t, 1H, J=7.6 Hz), 7.35-7.42 (m, 2H), 7.46 (d, 1H, J=8.4 Hz), 7.91 (d, 1H, J=7.6 Hz), 8.04 (s, 1H).

Compound II-70



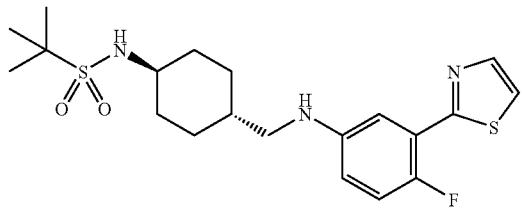
[Formula 238]

¹H-NMR (DMSO-d₆) δ: 0.93-1.05 (m, 2H), 1.10-1.32 (m, 2H), 1.26 (s, 9H), 1.42 (m, 1H), 1.78-1.86 (m, 2H), 1.86-1.95 (m, 2H), 2.78-2.83 (m, 2H), 3.03 (m, 1H), 4.80 (q, 2H, J=9.2 Hz), 5.48 (t, 1H, J=5.6 Hz), 6.69-6.76 (m, 2H), 7.08 (dd, 1H, J=8.8, 2.4 Hz), 7.45 (d, 1H, J=2.4 Hz).

377

Compound II-71

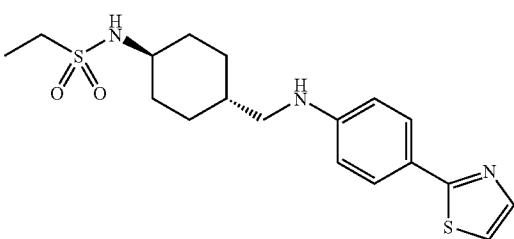
[Formula 239]



5

Compound II-76

[Formula 244]



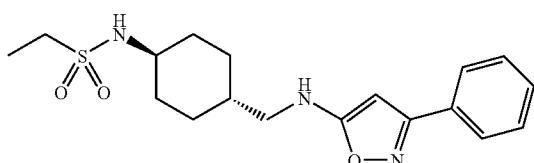
10

$^1\text{H-NMR}$ (DMSO-d₆) δ : 0.96-1.10 (m, 2H), 1.20-1.32 (m, 2H), 1.27 (s, 9H), 1.82-1.88 (m, 2H), 1.88-1.97 (m, 2H), 2.83-2.88 (m, 2H), 3.04 (m, 1H), 5.82 (s, 1H), 6.69 (m, 1H), 6.76 (d, 1H, $J=8.8$ Hz), 7.12 (dd, 1H, $J=9.2, 8.8$ Hz), 7.37 (m, 1H), 7.87 (d, 1H, $J=2.8$ Hz), 7.99 (s, 1H).

15

Compound II-72

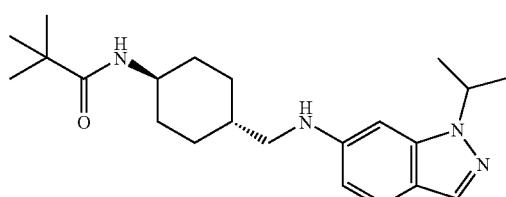
[Formula 240]



20

Compound II-77

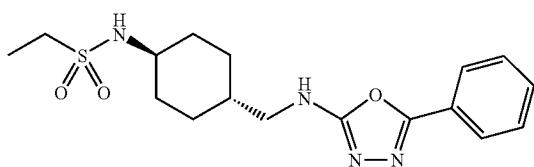
[Formula 245]



25

Compound II-73

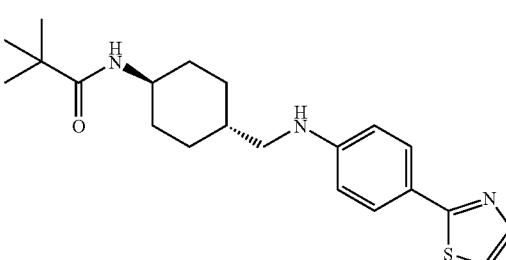
[Formula 241]



30

Compound II-78

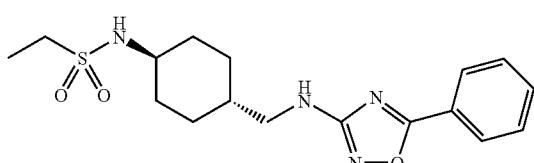
[Formula 246]



35

Compound II-74

[Formula 242]

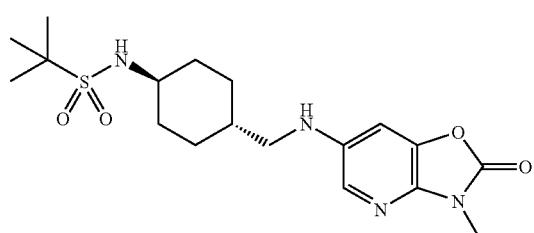


40

Compound II-79

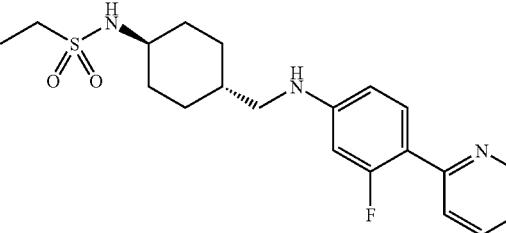
Compound II-75

[Formula 243]



55

[Formula 247]

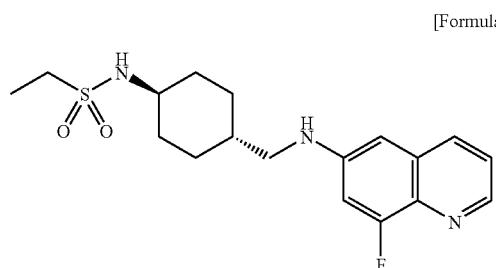


60

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379

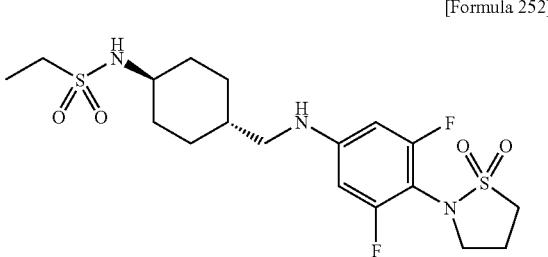
Compound II-80



[Formula 248]

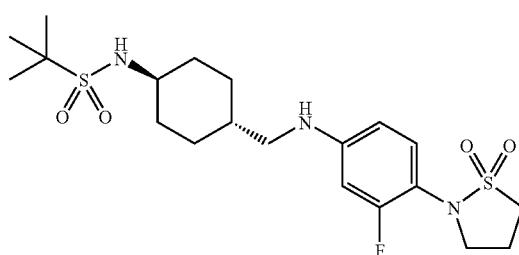
380

Compound II-84



[Formula 252]

Compound II-81

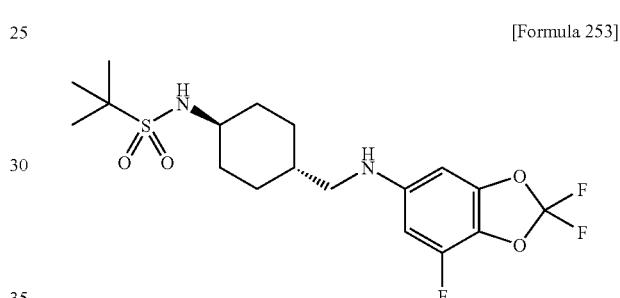


[Formula 249]

1H-NMR (DMSO-d₆) δ: 0.91-1.08 (m, 2H), 1.14-1.30 (t, 3H, J=7.5 Hz), 1.41 (m, 1H), 1.73-1.94 (m, 4H), 2.34-2.46 (m, 2H), 2.85 (t, 2H, J=6.6 Hz), 2.97 (q, 2H, J=7.5 Hz), 3.00 (m, 1H), 3.25 (t, 2H, J=7.5 Hz), 3.53 (t, 2H, J=6.6 Hz), 6.27 (d, 2H, J=11.7 Hz), 6.52 (t, 1H, J=5.1 Hz), 7.00 (d, 1H, J=7.2 Hz).

Compound II-85

Compound II-82

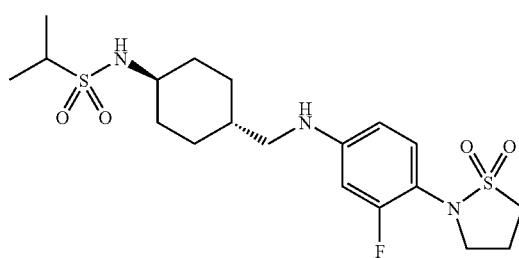


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[Formula 253]

[Formula 250]

Compound II-86



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[Formula 254]

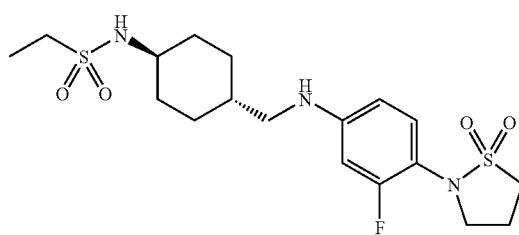
Compound II-83

Compound II-87

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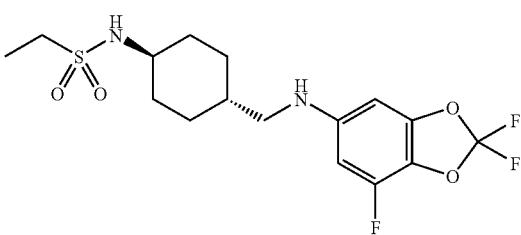
[Formula 251]

[Formula 255]



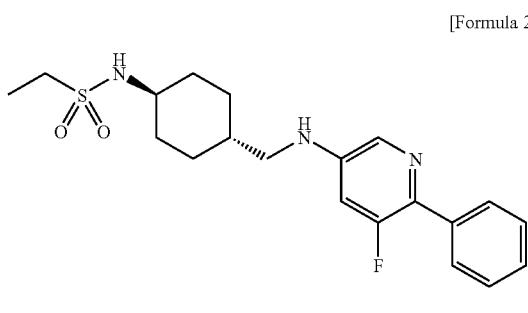
60

65

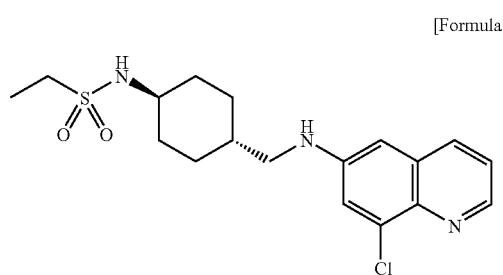


381

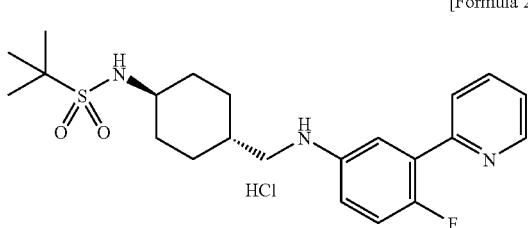
Compound II-88



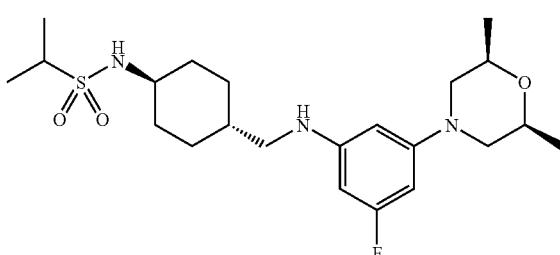
Compound II-89



Compound II-90



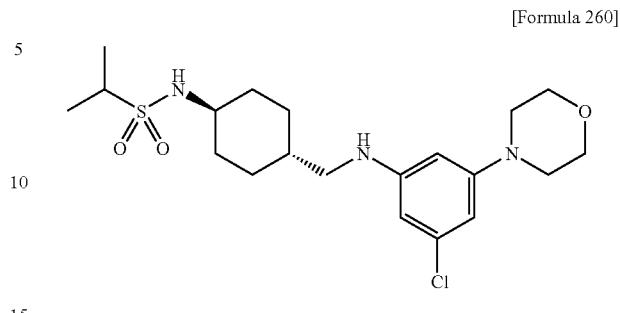
Compound II-91



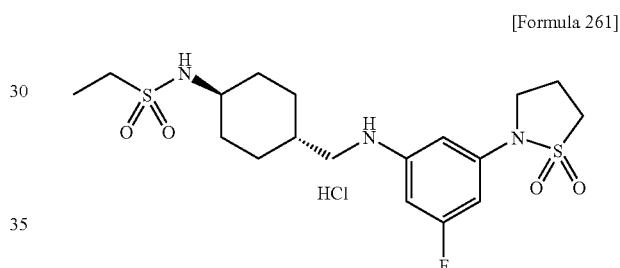
¹H-NMR (DMSO-d₆) δ: 0.92-1.05 (m, 2H), 1.13 (d, 6H, J=6.0 Hz), 1.18-1.30 (m, 2H), 1.21 (d, 6H, J=6.4 Hz), 1.40 (m, 1H), 1.76-1.83 (m, 2H), 1.83-1.93 (m, 2H), 2.19 (dd, 1H, J=11.2, 11.2 Hz), 2.76-2.82 (m, 2H), 3.01 (m, 1H), 3.09 (m, 1H), 3.45 (d, 2H, J=11.2 Hz), 3.58-3.69 (m, 2H), 5.67 (m, 1H), 5.77 (d, 1H, J=12.0 Hz), 5.90 (s, 1H), 5.91 (m, 1H), 6.91 (d, 1H, J=7.6 Hz).

382

Compound II-92

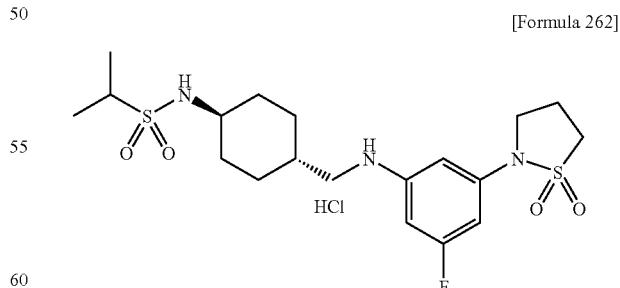


Compound II-93



¹H-NMR (DMSO-d₆) δ: 0.90-1.08 (m, 2H), 1.13-1.27 (m, 5H), 1.42 (m, 1H), 1.74-1.93 (m, 4H), 2.30-2.40 (m, 2H), 2.81 (d, 2H, J=6.6 Hz), 2.97 (q, 2H, J=7.5 Hz), 3.00 (m, 1H), 3.49 (t, 2H, J=7.5 Hz), 3.66 (t, 2H, J=6.6 Hz), 5.00-5.50 (brs, 2H), 6.07-6.15 (m, 2H), 6.25 (s, 1H), 7.00 (d, 1H, J=6.6 Hz).

Compound II-94

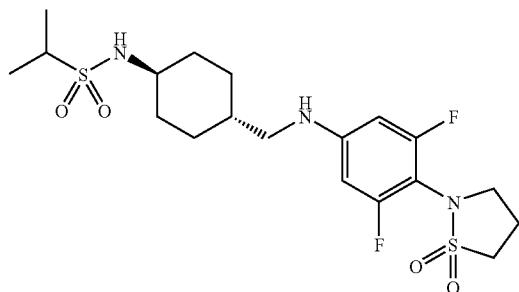


¹H-NMR (DMSO-d₆) δ: 0.92-1.07 (m, 2H), 1.15-1.32 (m, 5H), 1.21 (d, 6H, J=6.9 Hz), 1.42 (m, 1H), 1.74-1.93 (m, 4H), 2.30-2.42 (m, 2H), 2.81 (d, 2H, J=6.6 Hz), 2.92-3.18 (m, 2H), 3.49 (t, 2H, J=7.5 Hz), 3.66 (t, 2H, J=6.6 Hz), 4.70-5.30 (brs, 2H), 6.05-6.16 (m, 2H), 6.25 (s, 1H), 6.95 (d, 1H, J=8.1 Hz).

383

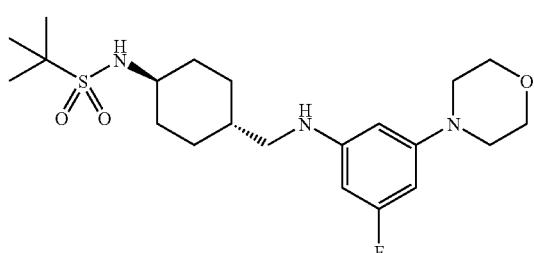
Compound II-95

[Formula 263]



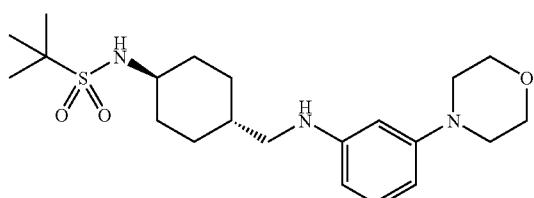
1H-NMR (DMSO-d₆) δ: 0.90-1.06 (m, 2H), 1.16-1.31 (d, 6H, J=6.9 Hz), 1.40 (m, 1H), 1.73-1.94 (m, 4H), 2.34-2.46 (m, 2H), 2.84 (t, 2H, J=6.0 Hz), 2.94-3.16 (m, 2H), 3.28 (t, 2H, J=7.5 Hz), 3.53 (t, 2H, J=6.6 Hz), 6.27 (d, 2H, J=11.7 Hz), 6.52 (t, 1H, J=5.4 Hz), 6.94 (d, 1H, J=7.8 Hz).

Compound II-96



1H-NMR (DMSO-d₆) δ: 0.91-1.04 (m, 2H), 1.20-1.32 (m, 2H), 1.26 (s, 9H), 1.40 (m, 1H), 1.76-1.95 (m, 4H), 2.77-2.83 (m, 2H), 2.99-3.04 (m, 5H), 3.67-3.72 (m, 4H), 5.71 (m, 1H), 5.79 (d, 1H, J=11.7 Hz), 5.89 (s, 1H), 5.90 (m, 1H), 6.72 (d, 1H, J=8.4 Hz).

Compound II-97



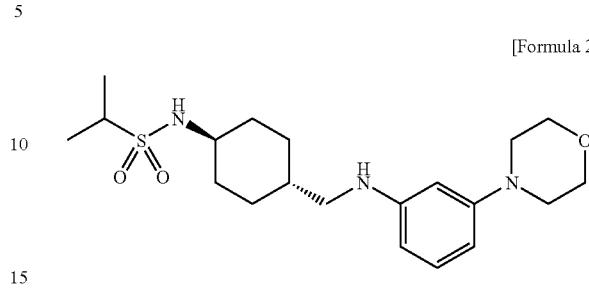
1H-NMR (DMSO-d₆) δ: 0.92-1.03 (m, 2H), 1.20-1.32 (m, 2H), 1.26 (s, 9H), 1.41 (m, 1H), 1.77-1.93 (m, 4H), 2.78-2.83 (m, 2H), 2.97-3.05 (m, 5H), 3.68-3.72 (m, 4H), 5.36 (m, 1H),

384

6.04 (d, 1H, J=8.0 Hz), 6.10 (s, 1H), 6.11 (d, 1H, J=8.0 Hz), 6.72 (d, 1H, J=8.0 Hz), 6.89 (dd, 1H, J=8.0, 8.0 Hz).

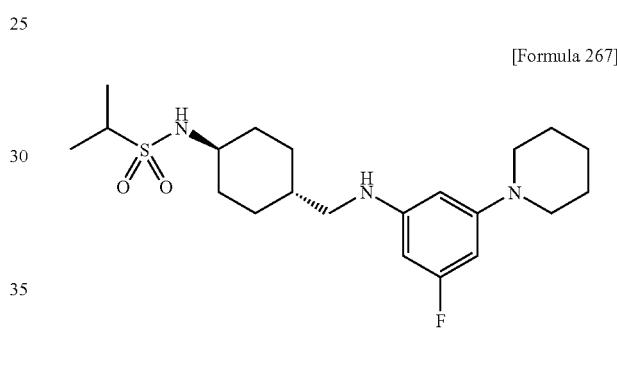
Compound II-98

[Formula 266]



1H-NMR (DMSO-d₆) δ: 0.92-1.04 (m, 2H), 1.17-1.29 (m, 2H), 1.21 (d, 6H, J=6.4 Hz), 1.41 (m, 1H), 1.75-1.92 (m, 4H), 2.77-2.83 (m, 2H), 2.95-3.05 (m, 5H), 3.09 (m, 1H), 3.67-3.72 (m, 4H), 5.36 (m, 1H), 6.04 (d, 1H, J=8.0 Hz), 6.10 (s, 1H), 6.11 (d, 1H, J=8.0 Hz), 6.89 (dd, 1H, J=8.0, 8.0 Hz), 6.92 (d, 1H, J=8.0 Hz).

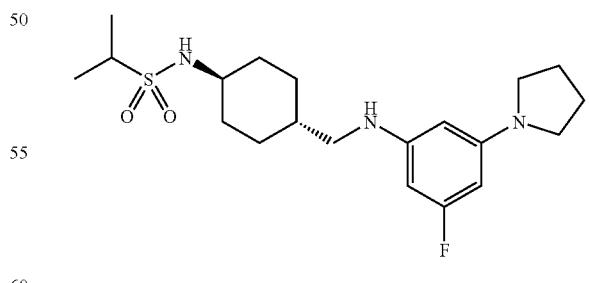
Compound II-99



1H-NMR (DMSO-d₆) δ: 0.90-1.06 (m, 2H), 1.15-1.31 (m, 2H), 1.21 (d, 6H, J=6.9 Hz), 1.39 (m, 1H), 1.47-1.62 (m, 6H), 1.74-1.94 (m, 4H), 2.78 (t, 2H, J=6.0 Hz), 2.93-3.16 (m, 6H), 5.64-5.76 (m, 2H), 5.83-5.92 (m, 2H), 6.94 (d, 1H, J=7.8 Hz).

Compound II-100

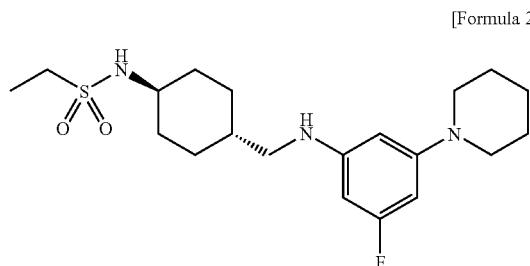
[Formula 268]



1H-NMR (DMSO-d₆) δ: 0.90-1.06 (m, 2H), 1.15-1.30 (m, 2H), 1.21 (d, 6H, J=6.9 Hz), 1.40 (m, 1H), 1.74-1.96 (m, 8H), 2.79 (t, 2H, J=6.0 Hz), 2.93-3.18 (m, 6H), 5.48-5.67 (m, 4H), 6.94 (d, 1H, J=8.1 Hz).

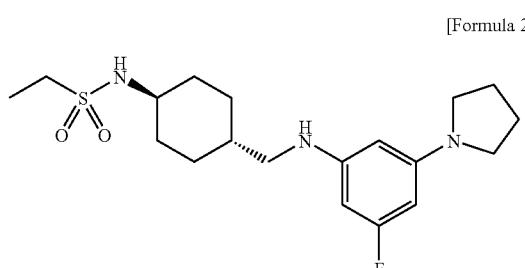
385

Compound Ii-101



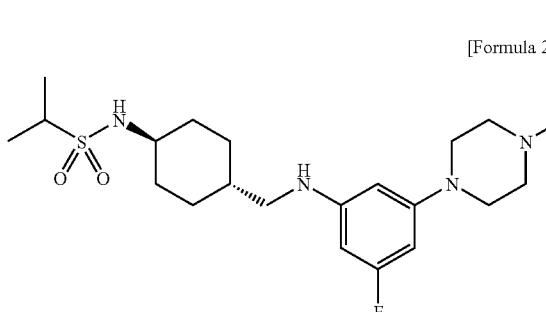
¹H-NMR (DMSO-d₆) δ: 0.90-1.06 (m, 2H), 1.13-1.29 (m, 2H), 1.18 (t, 3H, J=7.5 Hz), 1.39 (m, 1H), 1.47-1.62 (m, 6H), 1.75-1.94 (m, 4H), 2.79 (t, 2H, J=6.0 Hz), 2.97 (q, 2H, J=7.5 Hz), 3.03-3.10 (m, 4H), 5.64-5.75 (m, 2H), 5.83-5.91 (m, 2H), 7.00 (d, 1H, J=7.8 Hz).

Compound Ii-102



¹H-NMR (DMSO-d₆) δ: 0.90-1.07 (m, 2H), 1.13-1.29 (m, 2H), 1.18 (t, 3H, J=7.5 Hz), 1.41 (m, 1H), 1.74-1.96 (m, 8H), 2.79 (t, 2H, J=6.0 Hz), 2.97 (q, 2H, J=7.5 Hz), 3.00 (m, 1H), 3.09-3.19 (m, 4H), 5.46-5.66 (m, 4H), 6.99 (d, 1H, J=7.2 Hz).

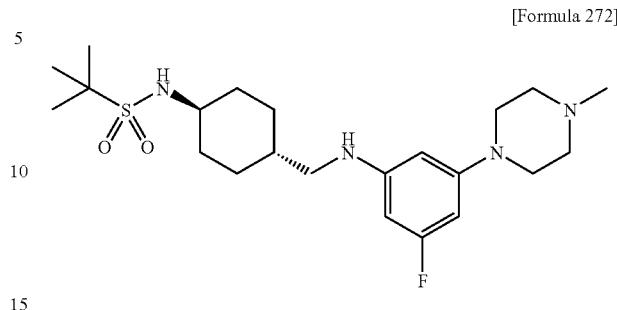
Compound Ii-103



1H-NMR (DMSO-d₆) δ: 0.91-1.03 (m, 2H), 1.16-1.29 (m, 2H), 1.21 (d, 6H, J=6.8 Hz), 1.40 (m, 1H), 1.75-1.92 (m, 4H), 2.20 (s, 3H), 2.35-2.43 (m, 4H), 2.75-2.82 (m, 2H), 2.88-3.13 (m, 6H), 5.67 (m, 1H), 5.76 (d, 1H, J=11.2 Hz), 5.82-5.92 (m, 2H), 6.91 (d, 1H, J=8.0 Hz).

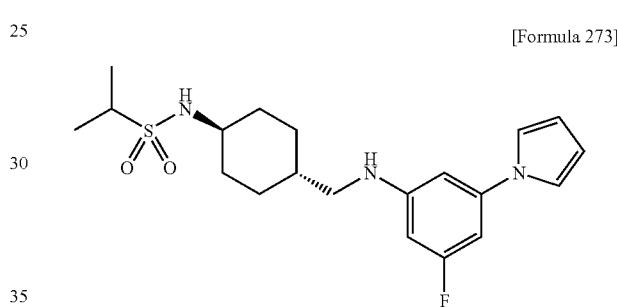
386

Compound Ii-104



¹H-NMR (DMSO-d₆) δ: 0.92-1.02 (m, 2H), 1.19-1.32 (m, 2H), 1.26 (s, 9H), 1.39 (m, 1H), 1.75-1.95 (m, 4H), 2.19 (s, 3H), 2.38-2.42 (m, 4H), 2.77-2.83 (m, 5H), 2.98-3.09 (m, 5H), 5.67 (m, 1H), 5.76 (d, 1H, J=11.2 Hz), 5.88 (m, 1H), 5.88 (s, 1H), 6.72 (d, 1H, J=8.8 Hz).

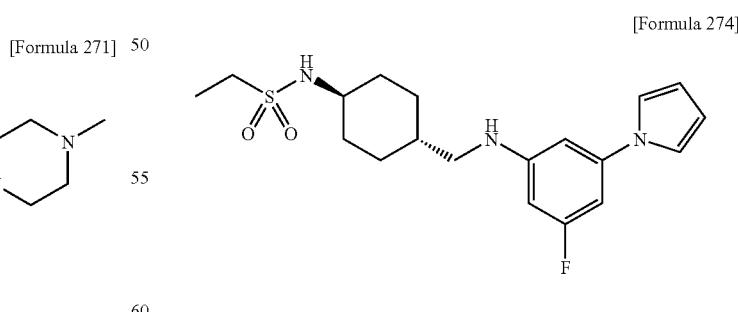
Compound Ii-105



⁴⁰ 1H-NMR (DMSO-d₆) δ: 0.95-1.09 (m, 2H), 1.18-1.31 (m, 2H), 1.22 (d, 6H, J=6.8 Hz), 1.44 (m, 1H), 1.78-1.93 (m, 4H), 2.87-2.92 (m, 2H), 3.03 (m, 1H), 3.10 (m, 1H), 6.13 (m, 1H), 6.21 (m, 1H), 6.22 (s, 2H), 6.51 (s, 1H), 6.52 (d, 1H, J=8.0 Hz), 6.92 (d, 1H, J=8.0 Hz), 7.26 (s, 2H).

⁴⁵

Compound Ii-106



¹H-NMR (DMSO-d₆) δ: 0.97-1.08 (m, 2H), 1.17-1.29 (m,
 65 5H), 1.40-1.68 (m, 3H), 1.80-1.92 (m, 2H), 2.90 (t, 2H, J=6.0
 Hz), 2.94-3.06 (m, 3H), 6.12-6.22 (m, 4H), 6.50-6.54 (m,
 2H), 6.94-7.00 (m, 1H), 7.26-7.27 (m, 2H).

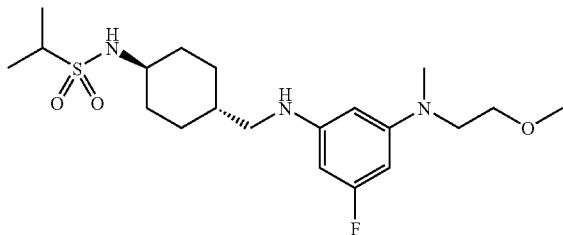
387

Compound II-107

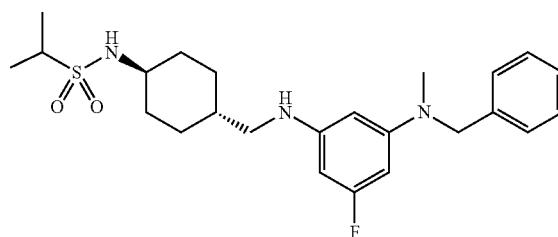
388

Compound II-110

[Formula 275]

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[Formula 278]



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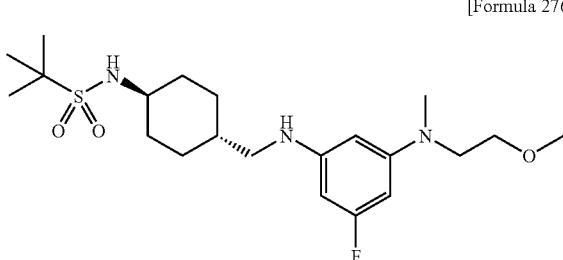
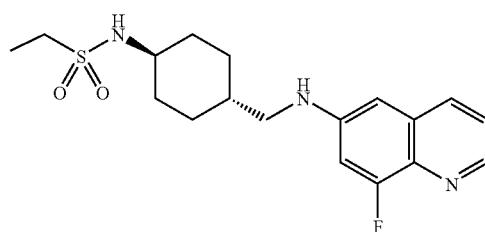
¹H-NMR (DMSO-d₆) δ: 0.91-1.03 (m, 2H), 1.16-1.29 (m, 2H), 1.21 (d, 6H, J=6.4 Hz), 1.40 (m, 1H), 1.74-1.92 (m, 4H), 2.75-2.81 (m, 2H), 2.84 (s, 3H), 3.00 (m, 1H), 3.09 (m, 1H), 3.25 (s, 3H), 3.35-3.47 (m, 4H), 5.59-5.67 (m, 4H), 6.91 (d, 1H, J=8.0 Hz).

Compound II-108

¹H-NMR (DMSO-d₆) δ: 0.83-1.01 (m, 2H), 1.00-1.40 (m, 3H), 1.21 (d, 6H, J=6.9 Hz), 1.68-1.91 (m, 4H), 2.73 (t, 2H, J=6.0 Hz), 2.90-3.15 (m, 2H), 2.95 (s, 3H), 4.48 (s, 2H), 5.60-5.72 (m, 4H), 6.94 (d, 1H, J=7.8 Hz), 7.15-7.35 (m, 5H). Compound II-111

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[Formula 279]

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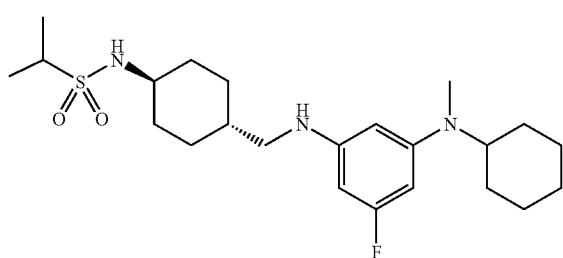
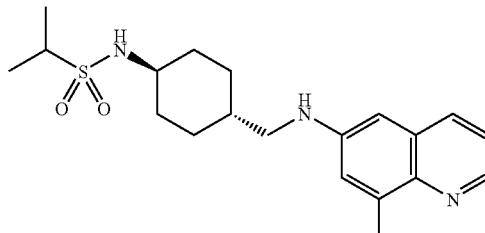
¹H-NMR (DMSO-d₆) δ: 0.97-1.14 (m, 2H), 1.14-1.33 (m, 5H), 1.45-1.61 (m, 1H), 1.81-1.96 (m, 4H), 2.90-3.10 (m, 5H), 6.34 (t, 1H, J=5.2 Hz), 6.51 (d, 1H, J=2.2 Hz), 6.99-7.07 (m, 2H), 7.36 (dd, 1H, J=8.2, 4.1 Hz), 8.02 (d, 1H, J=8.5 Hz), 8.48 (dd, 1H, J=4.1, 1.4 Hz). Compound II-112

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Compound II-109

[Formula 280]

[Formula 277]

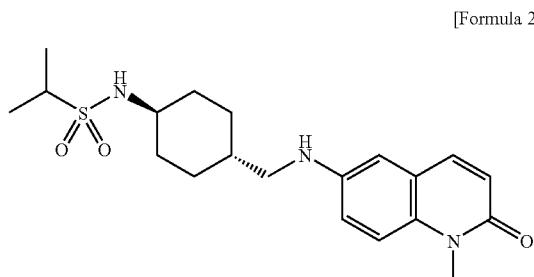
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¹H-NMR (DMSO-d₆) δ: 0.97-1.13 (m, 2H), 1.17-1.34 (m, 8H), 1.45-1.59 (m, 1H), 1.81-1.99 (m, 4H), 2.94 (t, 2H, J=5.9 Hz), 2.99-3.21 (m, 2H), 6.33 (t, 1H, J=5.4 Hz), 6.51 (d, 1H, J=2.2 Hz), 6.96 (d, 1H, J=7.7 Hz), 7.02 (dd, 1H, J=13.5, 2.2 Hz), 7.36 (dd, 1H, J=8.2, 4.1 Hz), 8.02 (d, 1H, J=8.5 Hz), 8.48 (dd, 1H, J=4.1, 1.4 Hz).

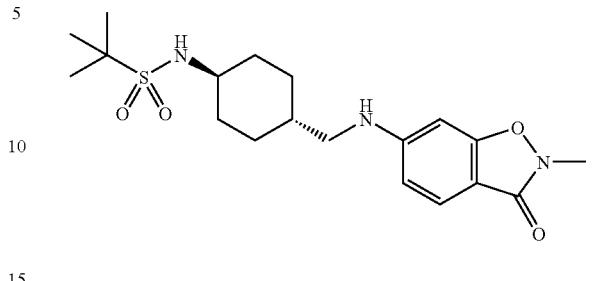
¹H-NMR (DMSO-d₆) δ: 0.90-1.51 (m, 10H), 1.21 (d, 6H, J=6.9 Hz), 1.56-1.67 (m, 3H), 1.71-1.93 (m, 6H), 2.64 (s, 3H), 2.78 (t, 2H, J=6.0 Hz), 2.93-3.17 (m, 2H), 3.44 (m, 1H), 5.56-5.77 (m, 4H), 6.94 (d, 1H, J=7.8 Hz).

389

Compound II-113



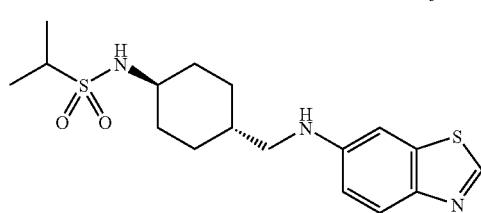
[Formula 281]



[Formula 284]

¹H-NMR (DMSO-d₆) δ: 0.93-1.13 (m, 2H), 1.15-1.34 (m, 8H), 1.39-1.57 (m, 1H), 1.79-1.95 (m, 4H), 2.87 (t, 2H, J=6.2 Hz), 2.94-3.16 (m, 2H), 3.54 (s, 3H), 5.66 (t, 1H, J=5.5 Hz), 6.49 (d, 1H, J=9.6 Hz), 6.73 (d, 1H, J=2.8 Hz), 6.91-7.02 (m, 2H), 7.29 (d, 1H, J=9.3 Hz), 7.72 (d, 1H, J=9.3 Hz).

Compound II-114

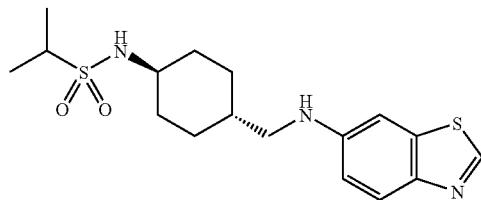


[Formula 282]

¹H-NMR (DMSO-d₆) δ: 0.95-1.07 (m, 4H), 1.26 (s, 9H), 1.39-1.47 (m, 1H), 1.80 (d, 2H, J=12.4 Hz), 1.91 (d, 2H, J=12.4 Hz), 2.87-2.93 (m, 2H), 2.98-3.06 (m, 1H), 3.37 (s, 3H), 6.27 (s, 1H), 6.55 (d, 1H, J=8.8 Hz), 6.73 (d, 1H, J=8.8 Hz), 6.80 (t, 1H, J=5.2 Hz), 7.32 (d, 1H, J=8.8 Hz).

Compound II-117

[Formula 285]

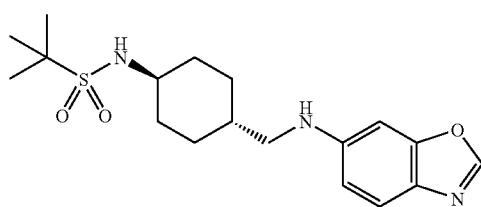


¹H-NMR (DMSO-d₆) δ: 0.93-1.10 (m, 2H), 1.14-1.33 (m, 8H), 1.41-1.56 (m, 1H), 1.79-1.94 (m, 4H), 2.89 (t, 2H, J=6.0 Hz), 2.95-3.16 (m, 2H), 6.00 (t, 1H, J=5.4 Hz), 6.84 (dd, 1H, J=8.8, 2.2 Hz), 6.95 (d, 1H, J=8.0 Hz), 7.07 (d, 1H, J=2.2 Hz), 7.72 (d, 1H, J=8.8 Hz), 8.86 (s, 11H).

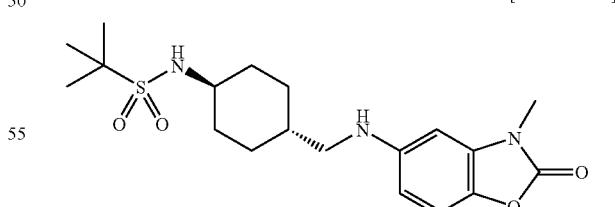
Compound II-115

¹H-NMR (DMSO-d₆) δ: 0.94-1.08 (m, 4H), 1.20 (s, 3H), 1.22 (s, 3H), 1.39-1.51 (m, 1H), 1.80 (d, 2H, J=12.4 Hz), 1.88 (d, 2H, J=12.4 Hz), 2.87-2.94 (m, 2H), 2.97-3.07 (m, 1H), 3.08-3.14 (m, 1H), 3.37 (s, 3H), 6.27 (s, 1H), 6.55 (d, 1H, J=8.4 Hz), 6.82 (t, 1H, J=5.6 Hz), 6.94 (d, 1H, J=8.0 Hz), 7.32 (d, 1H, J=8.4 Hz).

Compound II-118



[Formula 283]



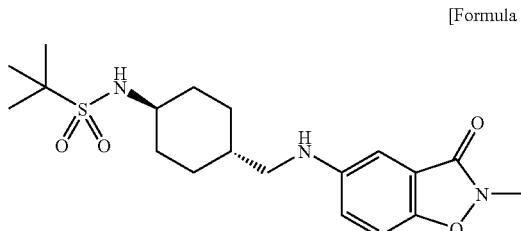
[Formula 286]

¹H-NMR (DMSO-d₆) δ: 0.94-1.06 (m, 4H), 1.26 (s, 9H), 1.40-1.51 (m, 1H), 1.84 (d, 2H, J=12.4 Hz), 1.91 (d, 2H, J=12.4 Hz), 2.85-2.90 (m, 2H), 2.97-3.06 (m, 1H), 5.93-5.99 (m, 1H), 6.63-6.79 (m, 3H), 7.40 (d, 1H, J=8.8 Hz), 8.32 (s, 1H).

¹H-NMR (DMSO-d₆) δ: 0.92-1.06 (m, 4H), 1.26 (s, 9H), 1.38-1.50 (m, 1H), 1.83 (d, 2H, J=12.4 Hz), 1.90 (d, 2H, J=12.4 Hz), 2.80-2.86 (m, 2H), 2.96-3.06 (m, 1H), 3.26 (s, 3H), 5.58-5.65 (m, 1H), 6.27 (d, 1H, J=8.4 Hz), 6.38 (s, 1H), 6.75 (d, 1H, J=8.4 Hz), 6.99 (d, 1H, J=8.4 Hz).

391

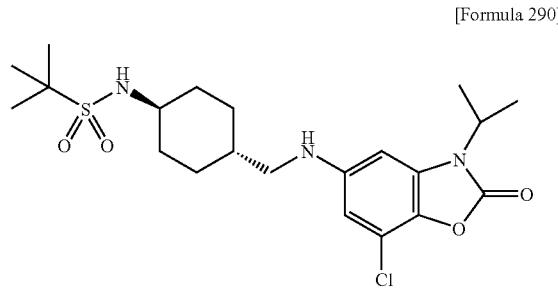
Compound II-119



[Formula 287]

392

Compound II-122



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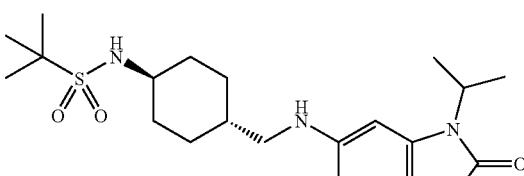
15

[Formula 290]

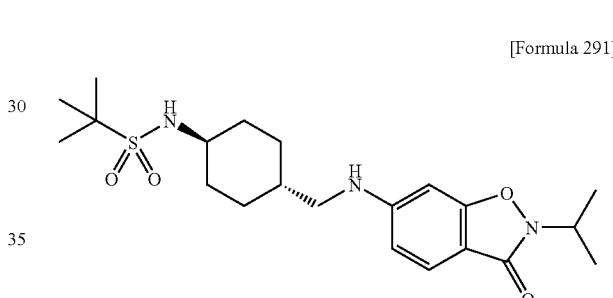
¹H-NMR (DMSO-d₆) δ: 0.94-1.06 (m, 4H), 1.26 (s, 9H), 1.39-1.50 (m, 1H), 1.84 (d, 2H, J=12.4 Hz), 1.90 (d, 2H, J=12.4 Hz), 2.81-2.89 (m, 2H), 2.96-3.07 (m, 1H), 3.51 (s, 3H), 5.79-5.84 (m, 1H), 6.60 (s, 1H), 6.75 (d, 1H, J=8.8 Hz), 7.03 (d, 1H, J=8.8 Hz), 7.19 (d, 1H, J=8.8 Hz).

Compound II-120

25 Compound II-123



[Formula 288]



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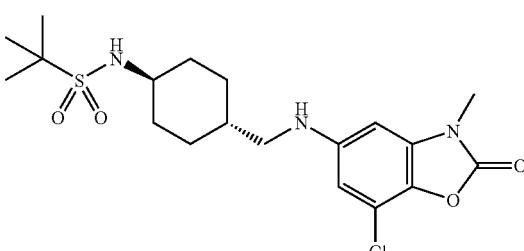
[Formula 291]

¹H-NMR (DMSO-d₆) δ: 0.93-1.10 (m, 4H), 1.26 (s, 9H), 1.37-1.40 (m, 1H), 1.42 (s, 3H), 1.44 (s, 3H), 1.83 (d, 2H, J=12.4 Hz), 1.91 (d, 2H, J=12.4 Hz), 2.79-2.96 (m, 2H), 2.97-3.07 (m, 1H), 4.33-4.46 (m, 1H), 5.50-5.59 (m, 1H), 6.25 (d, 1H, J=8.8 Hz), 6.57 (s, 1H), 6.75 (d, 1H, J=8.4 Hz), 7.00 (d, 1H, J=8.4 Hz).

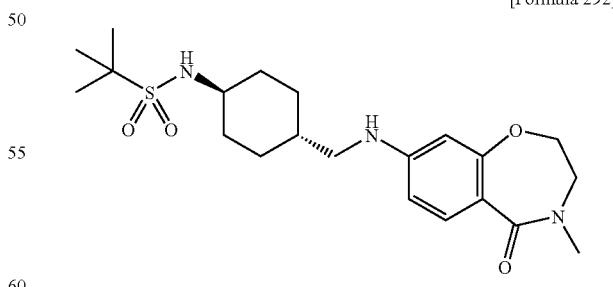
Compound II-121

¹H-NMR (DMSO-d₆) δ: 0.93-1.06 (m, 4H), 1.22 (s, 3H), 1.24 (s, 3H), 1.26 (s, 9H), 1.39-1.50 (m, 11H), 1.81 (d, 2H, J=12.4 Hz), 1.90 (d, 2H, J=12.4 Hz), 2.87-2.93 (m, 2H), 2.96-3.07 (m, 1H), 4.39-4.47 (m, 1H), 6.30 (s, 1H), 6.54 (d, 1H, J=8.8 Hz), 6.77 (d, 1H, J=8.8 Hz), 6.86 (t, 1H, J=5.2 Hz), 7.32 (d, 1H, J=8.4 Hz).

45 Compound II-124



[Formula 289]



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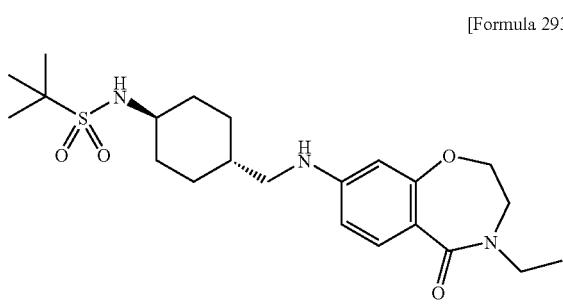
[Formula 292]

¹H-NMR (DMSO-d₆) δ: 0.90-1.06 (m, 4H), 1.26 (s, 9H), 1.36-1.49 (m, 1H), 1.82 (d, 2H, J=12.4 Hz), 1.90 (d, 2H, J=12.4 Hz), 2.80-2.87 (m, 2H), 2.95-3.97 (m, 1H), 3.27 (s, 3H), 5.85-5.92 (m, 1H), 6.33 (s, 1H), 6.36 (s, 1H), 6.75 (d, 1H, J=8.8 Hz).

¹H-NMR (DMSO-d₆) δ: 0.90-1.05 (m, 4H), 1.26 (s, 9H), 1.36-1.51 (m, 1H), 1.79 (d, 2H, J=12.4 Hz), 1.90 (d, 2H, J=12.4 Hz), 2.80-2.86 (m, 2H), 3.01 (s, 3H), 3.02-3.05 (m, 1H), 3.49 (t, 2H, J=4.8 Hz), 4.26 (t, 2H, J=4.8 Hz), 6.02 (s, 1H), 6.20 (t, 1H, J=5.6 Hz), 6.31 (d, 1H, J=8.8 Hz), 6.74 (d, 1H, J=8.8 Hz), 7.43 (d, 1H, J=8.4 Hz).

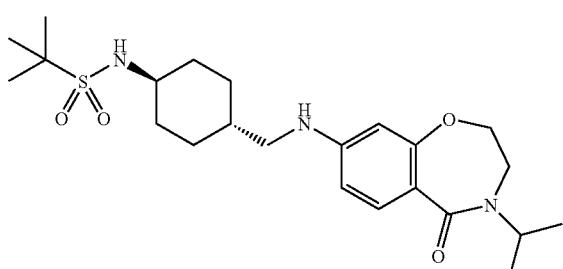
393

Compound II-125



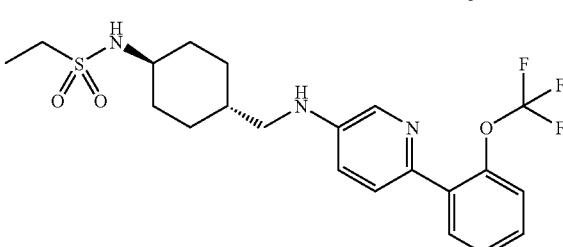
¹H-NMR (DMSO-d₆) δ: 0.92-1.02 (m, 4H), 1.08 (t, 3H, J=7.2 Hz), 1.25 (s, 9H), 1.35-1.42 (m, 1H), 1.79 (d, 2H, J=12.0 Hz), 1.90 (d, 2H, J=12.0 Hz), 2.80-2.86 (m, 2H), 2.96-3.05 (m, 1H), 3.42-3.51 (m, 4H), 4.20-4.26 (m, 2H), 6.03 (s, 1H), 6.20 (s, 1H), 6.31 (d, 1H, J=8.8 Hz), 6.75 (d, 1H, J=8.8 Hz), 7.42 (d, 1H, J=8.8 Hz).

Compound II-126



¹H-NMR (DMSO-d₆) δ: 0.92-1.02 (m, 4H), 1.09 (s, 3H), 1.11 (s, 3H), 1.25 (s, 9H), 1.43-1.55 (m, 1H), 1.80 (d, 2H, J=12.4 Hz), 1.91 (d, 2H, J=12.0 Hz), 2.84 (m, 2H), 2.97-3.08 (m, 1H), 3.37 (t, 2H, J=5.2 Hz), 4.18 (t, 2H, J=5.2 Hz), 4.71-4.80 (m, 1H), 6.05 (s, 1H), 6.19 (t, 1H, J=5.2 Hz), 6.32 (d, 1H, J=8.8 Hz), 6.74 (d, 1H, J=8.4 Hz), 7.18 (d, 1H, J=8.4 Hz).

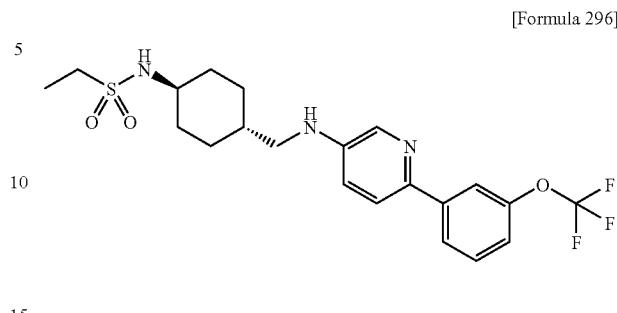
Compound II-127



¹H-NMR (DMSO-d₆) δ: 0.94-1.12 (m, 2H), 1.14-1.39 (m, 5H), 1.34-1.56 (m, 1H), 1.70-1.97 (m, 4H), 2.87-3.10 (m, 5H), 6.17 (t, 1H, J=5.2 Hz), 6.94-7.06 (m, 2H), 7.35-7.47 (m, 4H), 7.75-7.80 (m, 1H), 8.07 (d, 1H, J=3.0 Hz).

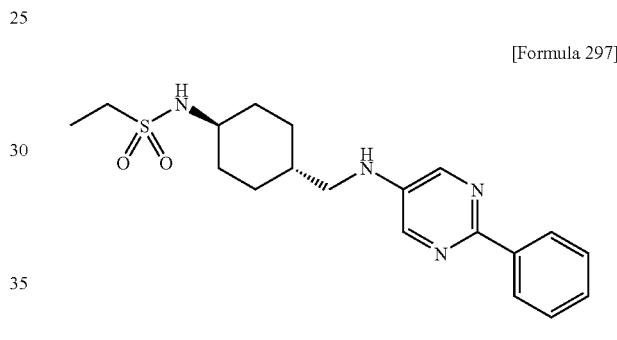
394

Compound II-128



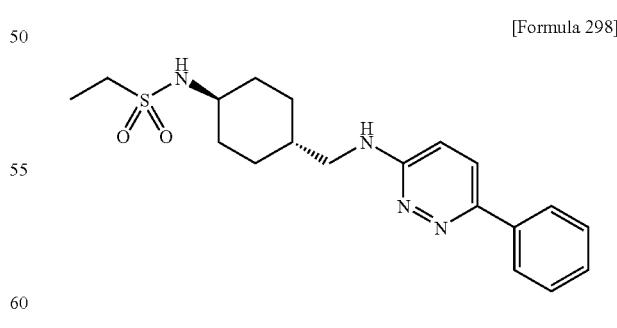
¹H-NMR (DMSO-d₆) δ: 0.96-1.12 (m, 2H), 1.14-1.31 (m, 5H), 1.31-1.55 (m, 1H), 1.70-1.96 (m, 4H), 2.89-3.09 (m, 5H), 6.24 (t, 1H, J=5.4 Hz), 6.94-7.05 (m, 2H), 7.24 (d, 1H, J=6.9 Hz), 7.52 (t, 1H, J=8.0 Hz), 7.75 (d, 1H, J=8.8 Hz), 7.88-7.97 (m, 2H), 8.07 (d, 1H, J=2.5 Hz).

Compound II-129



¹H-NMR (DMSO-d₆) δ: 0.98-1.12 (m, 2H), 1.18-1.30 (m, 2H), 1.19 (t, 3H, J=6.8 Hz), 1.48 (m, 1H), 1.79-1.95 (m, 4H), 2.92-3.09 (m, 3H), 2.97 (q, 2H, J=6.8 Hz), 6.27 (m, 1H), 7.01 (d, 1H, J=8.0 Hz), 7.39-7.47 (m, 2H), 7.56 (m, 1H), 8.18-8.25 (m, 2H), 8.23 (s, 2H).

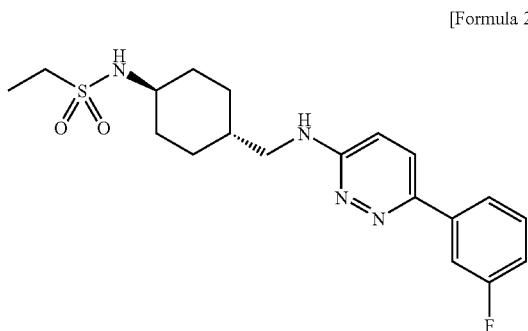
Compound II-130



¹H-NMR (DMSO-d₆) δ: 0.96-1.12 (m, 2H), 1.15-1.30 (m, 2H), 1.18 (t, 3H, J=7.2 Hz), 1.45-1.64 (m, 1H), 1.78-1.96 (m, 4H), 2.97 (q, 2H, J=7.2 Hz), 2.95-3.15 (m, 1H), 3.22-3.28 (m, 2H), 6.89 (d, 1H, J=9.0 Hz), 6.94-7.02 (m, 2H), 7.38 (t, 1H, J=6.0 Hz), 7.46 (t, 2H, J=7.5 Hz), 7.78 (d, 1H, J=9.0 Hz), 7.96 (d, 2H, J=9.0 Hz).

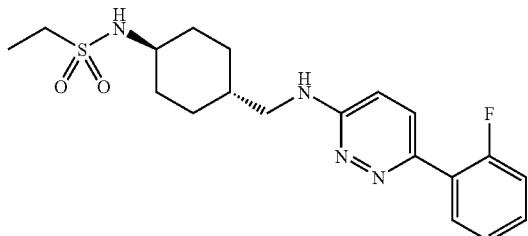
395

Compound II-131



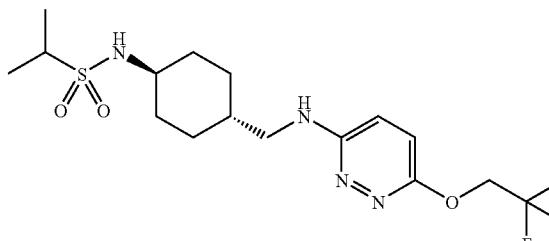
1H-NMR (DMSO-d₆) δ: 0.96-1.12 (m, 2H), 1.15-1.30 (m, 2H), 1.18 (t, 3H, J=7.2 Hz), 1.48-1.62 (m, 1H), 1.78-1.96 (m, 4H), 2.98 (q, 2H, J=7.2 Hz), 2.94-3.10 (m, 1H), 3.22-3.28 (m, 2H), 6.89 (d, 1H, J=9.0 Hz), 7.02 (d, 1H, J=9.0 Hz), 7.10 (t, 1H, J=5.4 Hz), 7.22 (td, 1H, J=9.0, 3.0 Hz), 7.47-7.56 (m, 1H), 7.77-7.88 (m, 3H).

Compound II-132



1H-NMR (DMSO-d₆) δ: 0.96-1.13 (m, 2H), 1.15-1.32 (m, 2H), 1.19 (t, 3H, J=7.5 Hz), 1.48-1.65 (m, 1H), 1.78-1.96 (m, 4H), 2.98 (q, 2H, J=7.2 Hz), 2.94-3.12 (m, 1H), 3.22-3.28 (m, 2H), 6.89 (d, 1H, J=9.0 Hz), 7.01 (d, 1H, J=6.0 Hz), 7.09 (t, 1H, J=5.4 Hz), 7.27-7.35 (m, 2H), 7.42-7.50 (m, 1H), 7.57 (dd, 1H, J=9.0, 3.0 Hz), 7.86 (td, 1H, J=7.5, 3.0 Hz).

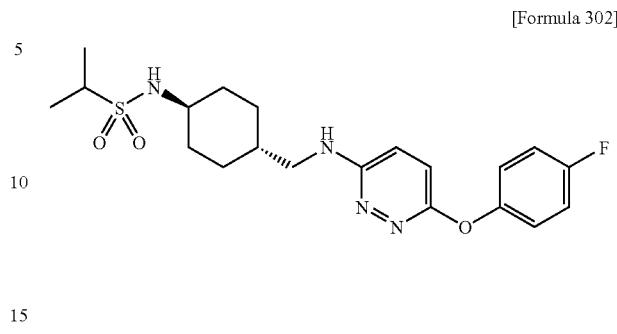
Compound II-133



1H-NMR (DMSO-d₆) δ: 0.92-1.08 (m, 2H), 1.15-1.30 (m, 2H), 1.21 (d, 6H, J=6.6 Hz), 1.42-1.58 (m, 1H), 1.72-1.94 (m, 4H), 2.95-3.20 (m, 4H), 4.89-4.98 (m, 2H), 6.65 (brs, 1H), 6.92 (d, 1H, J=9.0 Hz), 6.91-6.98 (m, 1H), 7.03 (d, 1H, J=9.0 Hz).

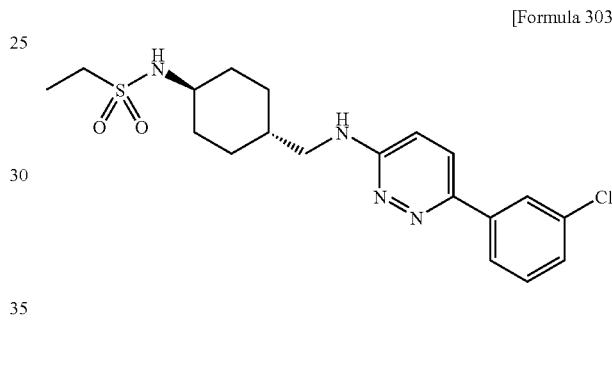
396

Compound II-134



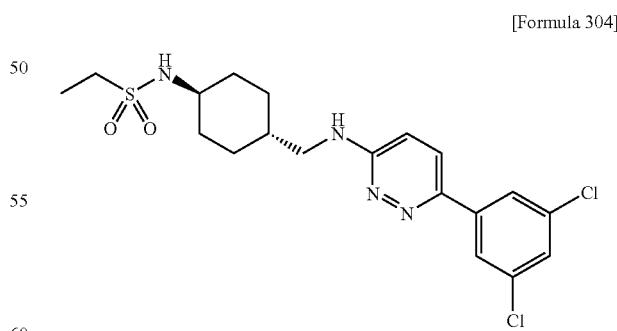
1H-NMR (DMSO-d₆) δ: 0.90-1.08 (m, 2H), 1.15-1.30 (m, 2H), 1.21 (d, 6H, J=6.6 Hz), 1.42-1.58 (m, 1H), 1.72-1.94 (m, 4H), 2.92-3.20 (m, 4H), 6.74 (t, 1H, J=6.0 Hz), 6.94 (t, 1H, J=6.0 Hz), 6.97 (s, 1H), 7.08-7.24 (m, 5H).

Compound II-135



1H-NMR (DMSO-d₆) δ: 0.95-1.10 (m, 2H), 1.12-1.30 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.48-1.60 (m, 1H), 1.76-1.94 (m, 4H), 2.92-3.10 (m, 1H), 2.97 (q, 2H, J=7.2 Hz), 3.18-3.30 (m, 2H), 6.89 (d, 1H, J=9.6 Hz), 7.02 (brs, 1H), 7.11 (t, 1H, J=5.4 Hz), 7.42-7.56 (m, 2H), 7.85 (d, 1H, J=9.6 Hz), 7.93 (d, 1H, J=7.5 Hz), 8.03 (s, 1H).

Compound II-136

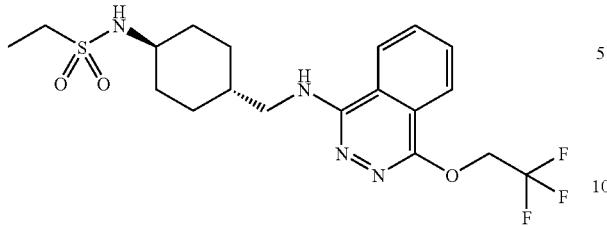


1H-NMR (DMSO-d₆) δ: 0.98-1.12 (m, 2H), 1.13-1.30 (m, 2H), 1.18 (t, 3H, J=7.2 Hz), 1.48-1.62 (m, 1H), 1.78-1.96 (m, 4H), 2.92-3.12 (m, 1H), 2.97 (q, 2H, J=7.2 Hz), 3.22-3.32 (m, 2H), 6.89 (d, 1H, J=9.0 Hz), 7.01 (d, 1H, J=7.5 Hz), 7.20 (t, 1H, J=6.0 Hz), 7.62 (s, 1H), 7.91 (d, 1H, J=9.0 Hz), 8.02 (s, 2H).

397

Compound II-137

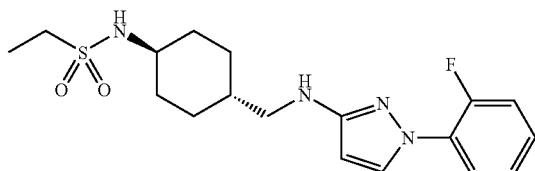
[Formula 305]



¹H-NMR (DMSO-d₆) δ: 0.95-1.12 (m, 2H), 1.13-1.30 (m, 2H), 1.18 (t, 3H, J=7.2 Hz), 1.65-1.95 (m, 5H), 2.93-3.12 (m, 1H), 2.97 (q, 2H, J=7.2 Hz), 3.25-3.40 (m, 2H), 5.07-5.16 (m, 2H), 7.01 (d, 1H, J=7.5 Hz), 7.25 (t, 1H, J=6.0 Hz), 7.92-8.03 (m, 3H), 8.33 (d, 1H, J=6.0 Hz).

Compound II-138

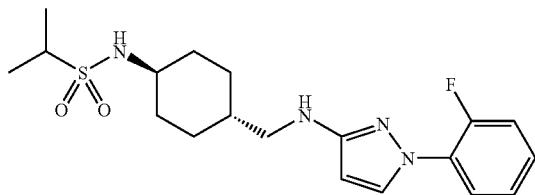
[Formula 306]



¹H-NMR (DMSO-d₆) δ: 0.91-1.26 (m, 4H), 1.19 (t, 3H, J=7.5 Hz), 1.36-1.43 (m, 1H), 1.78-1.90 (m, 4H), 2.90-3.07 (m, 3H), 2.96 (q, 2H, J=7.5 Hz), 5.69 (t, 1H, J=5.7 Hz), 5.81 (d, 1H, J=2.4 Hz), 7.00 (d, 1H, J=7.8 Hz), 7.16-7.39 (m, 3H), 7.73-7.79 (m, 1H), 7.86-7.88 (m, 1H).

Compound II-139

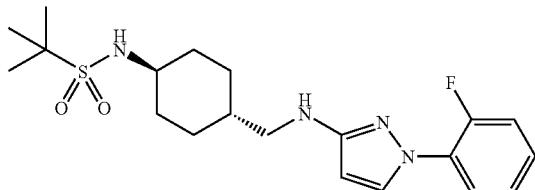
[Formula 307]



¹H-NMR (DMSO-d₆) δ: 0.90-1.06 (m, 4H), 1.20 (s, 3H), 1.22 (s, 3H), 1.40-1.52 (m, 1H), 1.81 (d, 2H, J=12.4 Hz), 1.88 (d, 2H, J=12.4 Hz), 2.90-2.98 (m, 2H), 2.99-3.13 (m, 2H), 5.68 (t, 1H, J=5.6 Hz), 5.81 (s, 1H), 6.93 (d, 1H, J=8.8 Hz), 7.16-7.40 (m, 3H), 7.76 (t, 1H, J=8.0 Hz), 7.87 (s, 1H).

Compound II-140

[Formula 308]

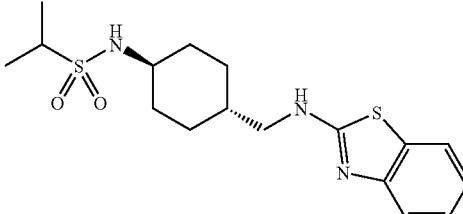


¹H-NMR (DMSO-d₆) δ: 0.90-1.06 (m, 4H), 1.26 (s, 9H), 1.40-1.49 (m, 1H), 1.82 (d, 2H, J=12.4 Hz), 1.91 (d, 2H, J=12.4 Hz), 2.90-2.99 (m, 2H), 3.01-3.06 (m, 1H), 5.67 (t, 1H, J=6.0 Hz), 5.81 (s, 1H), 6.74 (d, 1H, J=8.4 Hz), 7.14-7.40 (m, 3H), 7.76 (t, 1H, J=8.4 Hz), 7.87 (s, 1H).

398

Compound II-141

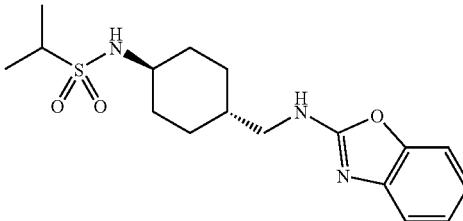
[Formula 309]



¹H-NMR (DMSO-d₆) δ: 0.97-1.06 (m, 2H), 1.18-1.27 (m, 2H), 1.21 (d, 6H, J=6.9 Hz), 1.45-1.59 (m, 1H), 1.76-1.81 (m, 2H), 1.87-1.91 (m, 2H), 2.97-3.09 (m, 1H), 3.10-3.13 (m, 1H), 3.17-3.22 (m, 2H), 6.94-7.02 (m, 2H), 6.98 (td, 1H, J=7.8, 1.2 Hz), 7.36 (dd, 1H, J=7.8, 0.6 Hz), 7.65 (dd, 1H, J=7.8, 0.6 Hz), 8.00-8.05 (m, 1H).

Compound II-142

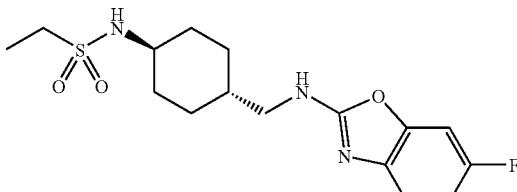
[Formula 310]



¹H-NMR (DMSO-d₆) δ: 0.96-1.04 (m, 2H), 1.18-1.28 (m, 2H), 1.20 (d, 6H, J=6.9 Hz), 1.43-1.59 (m, 1H), 1.74-1.79 (m, 2H), 1.85-1.90 (m, 2H), 2.92-3.07 (m, 1H), 3.09-3.18 (m, 3H), 6.92-6.99 (m, 2H), 7.10 (td, 1H, J=7.8, 1.2 Hz), 7.21 (dd, 1H, J=7.8, 0.6 Hz), 7.31 (dd, 1H, J=7.8, 0.6 Hz), 7.89-7.97 (m, 1H).

Compound II-143

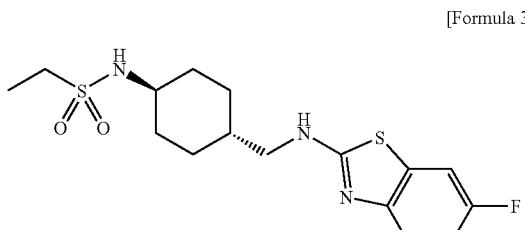
[Formula 311]



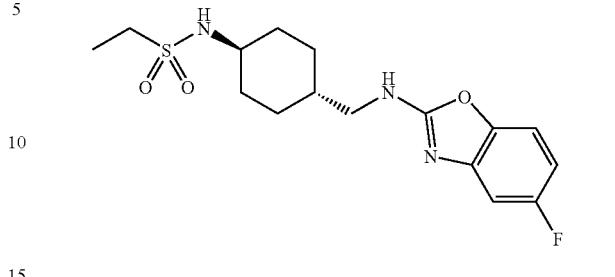
¹H-NMR (DMSO-d₆) δ: 0.97-1.07 (m, 2H), 1.17-1.23 (m, 2H), 1.18 (t, 3H, J=7.2 Hz), 1.42-1.57 (m, 1H), 1.73-1.78 (m, 2H), 1.86-1.90 (m, 2H), 2.93-3.02 (m, 1H), 2.97 (q, 2H, J=7.2 Hz), 3.11 (t, 2H, J=6.3 Hz), 6.91-7.02 (m, 2H), 7.19 (dd, 1H, J=8.4, 4.8. Hz), 7.34 (dd, 1H, J=9.3, 2.4 Hz), 8.00 (t, 1H, J=6.0 Hz).

399

Compound II-144



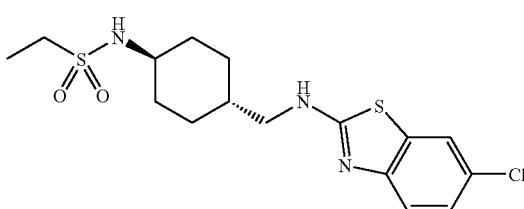
[Formula 312]



[Formula 315]

¹H-NMR (DMSO-d₆) δ: 0.97-1.08 (m, 2H), 1.16-1.24 (m, 2H), 1.18 (t, 3H, J=7.2 Hz), 1.42-1.59 (m, 1H), 1.74-1.80 (m, 2H), 1.85-1.90 (m, 2H), 2.92-3.03 (m, 1H), 2.97 (q, 2H, J=7.5 Hz), 3.18 (t, 2H, J=6.3 Hz), 6.99-7.07 (m, 2H), 7.33 (dd, 1H, J=9.0, 4.8 Hz), 7.58 (dd, 1H, J=8.7, 2.7 Hz), 8.00 (t, 1H, J=5.4 Hz).

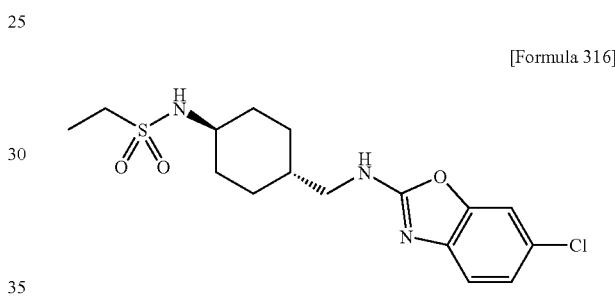
Compound II-145



[Formula 313]

¹H-NMR (DMSO-d₆) δ: 0.98-1.04 (m, 2H), 1.16-1.23 (m, 2H), 1.18 (t, 3H, J=7.2 Hz), 1.43-1.59 (m, 1H), 1.73-1.78 (m, 2H), 1.86-1.89 (m, 2H), 2.93-3.00 (m, 3H), 3.11-3.15 (m, 2H), 6.72-6.79 (m, 1H), 7.00-7.08 (m, 2H), 7.29-7.34 (m, 1H), 8.13-8.16 (m, 1H).

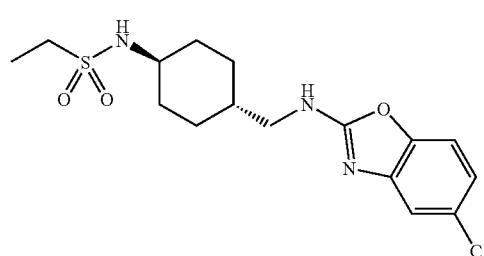
Compound II-148



[Formula 316]

¹H-NMR (DMSO-d₆) δ: 0.97-1.09 (m, 2H), 1.17-1.23 (m, 2H), 1.18 (t, 3H, J=7.2 Hz), 1.43-1.59 (m, 1H), 1.72-1.81 (m, 2H), 1.85-1.92 (m, 2H), 2.95-3.06 (m, 1H), 2.97 (q, 2H, J=7.5 Hz), 3.19 (t, 2H, J=6.0 Hz), 7.01 (d, 1H, J=8.1 Hz), 7.20-7.23 (m, 1H), 7.33 (dd, 1H, J=8.7, 0.6 Hz), 7.58 (dd, 1H, J=2.1, 0.9 Hz), 8.11-8.18 (m, 1H).

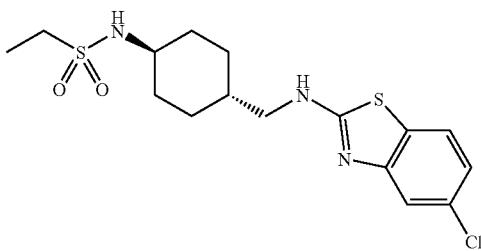
Compound II-146



[Formula 314]

¹H-NMR (DMSO-d₆) δ: 0.94-1.06 (m, 2H), 1.15-1.26 (m, 2H), 1.18 (t, 3H, J=7.2 Hz), 1.45-1.58 (m, 1H), 1.72-1.80 (m, 2H), 1.84-1.92 (m, 2H), 2.96 (q, 2H, J=7.2 Hz), 2.96-3.05 (m, 1H), 3.09-3.16 (m, 2H), 6.99 (d, 1H, J=8.0 Hz), 7.13 (dd, 1H, J=8.0, 2.0 Hz), 7.20 (d, 1H, J=8.4 Hz), 7.49 (d, 1H, J=2.0 Hz), 8.11 (t, 1H, J=6.0 Hz).

Compound II-149



[Formula 317]

¹H-NMR (DMSO-d₆) δ: 0.98-1.06 (m, 2H), 1.15-1.21 (m, 2H), 1.18 (t, 3H, J=7.2 Hz), 1.42-1.58 (m, 1H), 1.70-1.81 (m, 2H), 1.82-1.96 (m, 2H), 2.93-3.00 (m, 3H), 3.13-3.19 (m, 2H), 6.98-7.02 (m, 2H), 7.26-7.27 (m, 1H), 7.32-7.35 (m, 1H), 8.18-8.21 (m, 1H).

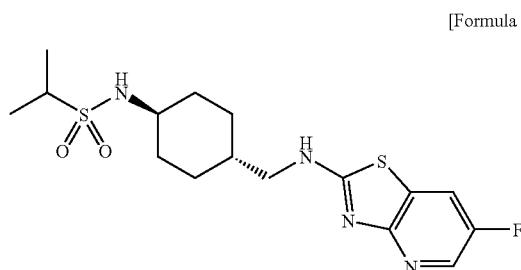
¹H-NMR (DMSO-d₆) δ: 0.96-1.08 (m, 2H), 1.12-1.24 (m, 2H), 1.18 (t, 3H, J=7.2 Hz), 1.43-1.59 (m, 1H), 1.74-1.80 (m, 2H), 1.86-1.91 (m, 2H), 2.93-3.01 (m, 3H), 3.17-3.22 (m, 2H), 7.00-7.05 (m, 2H), 7.37-7.39 (m, 1H), 7.65-7.68 (m, 1H), 8.22-8.26 (m, 1H).

400

Compound II-147

401

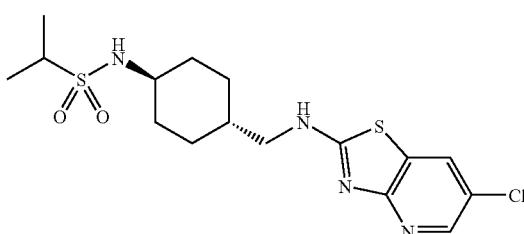
Compound II-150



[Formula 318]

1H-NMR (DMSO-d₆) δ: 0.98-1.08 (m, 2H), 1.15-1.29 (m, 2H), 1.21 (d, 6H, J=6.9 Hz), 1.44-1.60 (m, 1H), 1.74-1.80 (m, 2H), 1.86-1.91 (m, 2H), 2.95-3.17 (m, 2H), 3.21-3.27 (m, 2H), 6.95-6.98 (m, 1H), 8.10 (dd, 1H, J=8.4, 2.7 Hz), 8.19 (dd, 1H, J=3.0, 1.5 Hz), 8.44-8.47 (m, 1H).

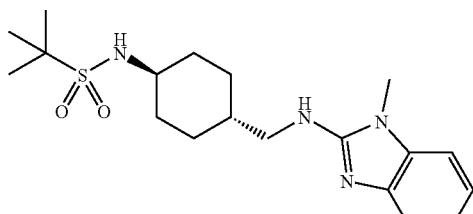
Compound II-151



[Formula 319]

1H-NMR (DMSO-d₆) δ: 0.99-1.04 (m, 2H), 1.15-1.23 (m, 2H), 1.21 (d, 6H, J=6.3 Hz), 1.43-1.59 (m, 1H), 1.73-1.81 (m, 2H), 1.85-1.91 (m, 2H), 2.97-3.18 (m, 2H), 3.21-3.29 (m, 2H), 6.95-6.98 (m, 1H), 8.20-8.23 (m, 2H), 8.58-8.61 (m, 1H).

Compound II-152



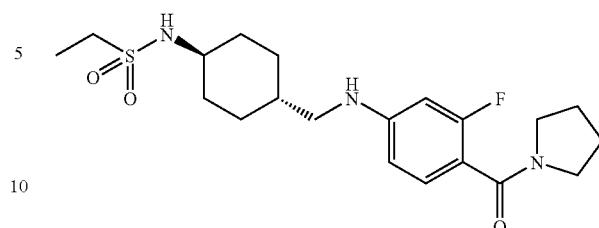
[Formula 320]

1H-NMR (DMSO-d₆) δ: 0.96-1.04 (m, 2H), 1.15-1.26 (m, 2H), 1.25 (s, 9H), 1.56-1.62 (m, 1H), 1.78-1.83 (m, 2H), 1.87-1.93 (m, 2H), 2.98-3.08 (m, 1H), 3.17 (t, 2H, J=6.3 Hz), 3.48 (s, 3H), 6.47 (d, 2H, J=8.7 Hz), 6.89-6.96 (m, 2H), 7.11-7.19 (m, 2H).

402

Compound II-153

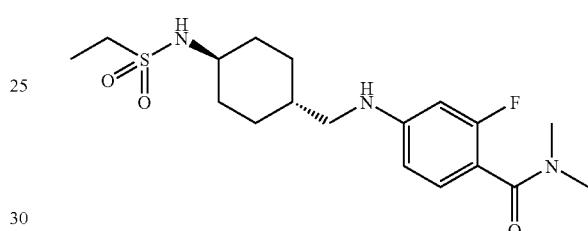
[Formula 321]



1H-NMR (DMSO-d₆) δ: 0.95-1.04 (m, 2H), 1.13-1.30 (m, 2H), 1.18 (t, 3H, J=7.5 Hz), 1.41 (m, 1H), 1.71-1.94 (m, 4H), 2.80-2.89 (m, 2H), 2.92-3.10 (m, 2H), 2.97 (q, 2H, J=7.5 Hz), 3.21-3.30 (m, 2H), 6.25-6.35 (m, 2H), 6.39 (dd, 1H, J=8.4, 2.1 Hz), 7.01 (d, 1H, J=7.5 Hz), 7.01 (dd, 1H, J=8.4, 8.4 Hz).

Compound II-154

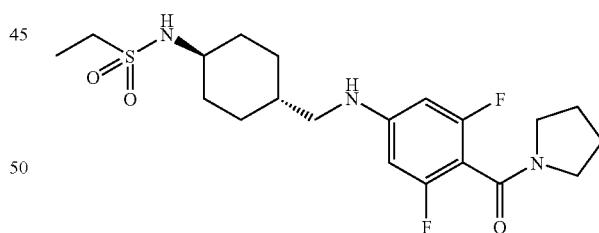
[Formula 322]



1H-NMR (DMSO-d₆) δ: 0.91-1.09 (m, 2H), 1.16-1.28 (m, 2H), 1.18 (t, 3H, J=7.5 Hz), 1.42 (m, 1H), 1.74-1.95 (m, 4H), 2.80-3.16 (m, 9H), 2.97 (q, 2H, J=7.5 Hz), 6.24-6.36 (m, 2H), 6.30 (dd, 1H, J=8.4, 2.1 Hz), 7.10 (dd, 1H, J=8.4, 2.1 Hz), 7.05 (d, 1H, J=8.4 Hz).

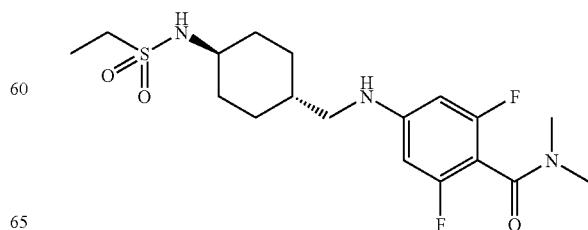
Compound II-155

[Formula 323]



Compound II-156

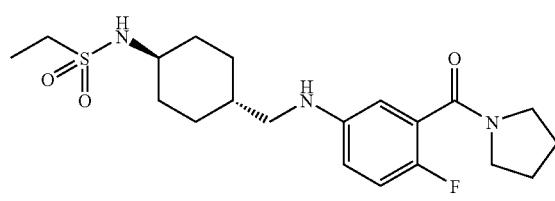
[Formula 324]



403

Compound II-157

[Formula 325]

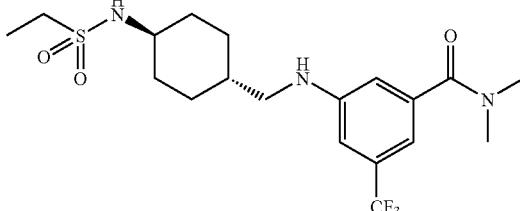


5

404

Compound II-162

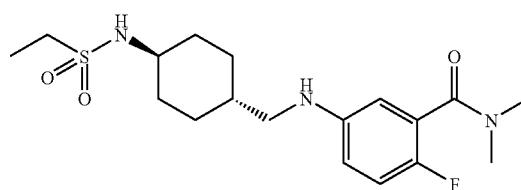
[Formula 330]



10

Compound II-158

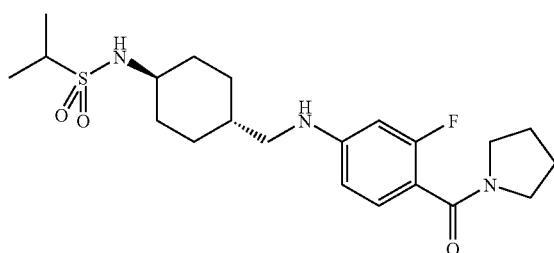
[Formula 326]



15

Compound II-163

[Formula 331]

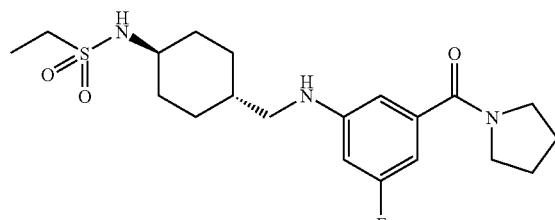


20

¹H-NMR (DMSO-d₆) δ: 0.91-1.07 (m, 2H), 1.10-1.30 (m, 5H), 1.41 (m, 1H), 1.76-1.94 (m, 4H), 2.74-2.83 (m, 2H), 2.83 (s, 3H), 2.90-3.08 (m, 3H), 2.96 (s, 3H), 5.68 (m, 1H), 6.39 (m, 1H), 6.58 (m, 1H), 6.95 (dd, 1H, J=8.4, 8.4 Hz), 7.00 (d, 1H, J=7.8 Hz).

Compound II-159

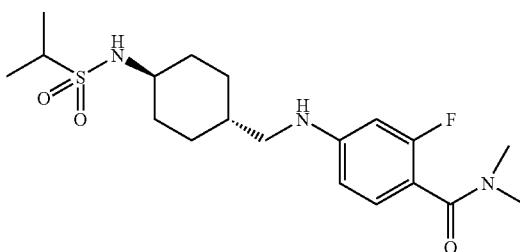
[Formula 327]



25

Compound II-164

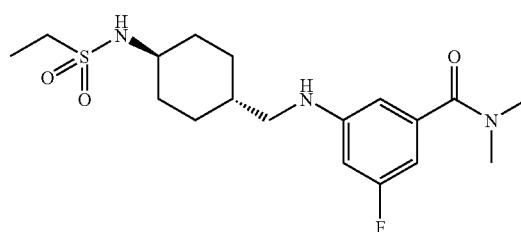
[Formula 332]



30

Compound II-160

[Formula 328]



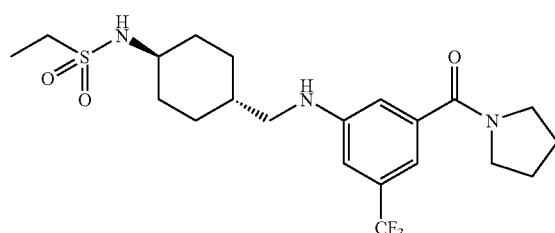
35

Compound II-165

40

Compound II-161

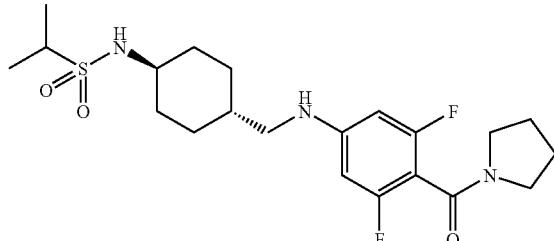
[Formula 329]



45

50

[Formula 333]



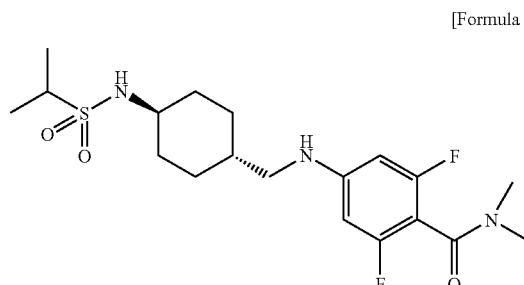
55

60

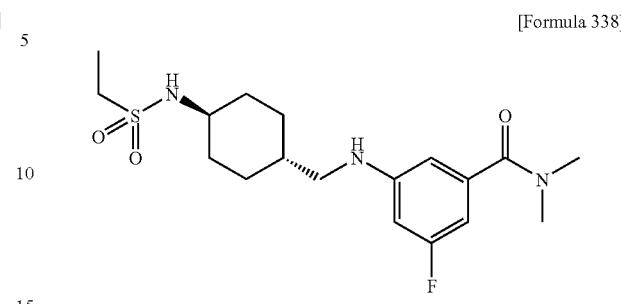
65

405

Compound II-166

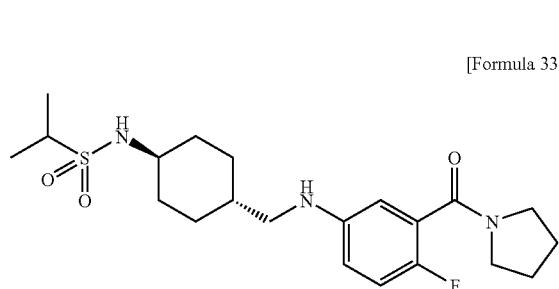
**406**

Compound II-170



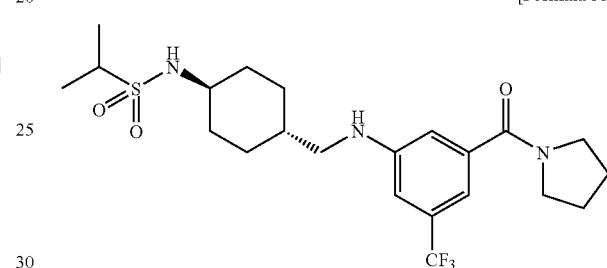
Compound II-171

Compound II-167



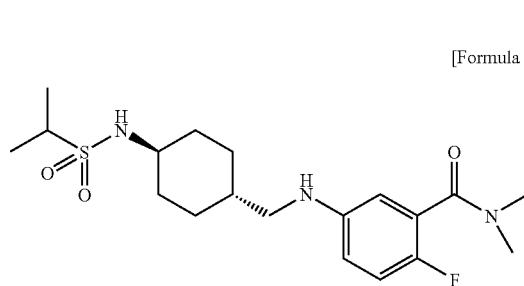
20

[Formula 339]



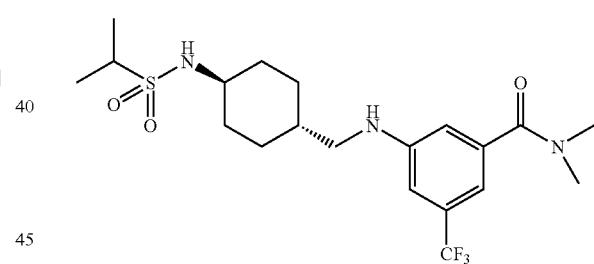
Compound II-172

Compound II-168



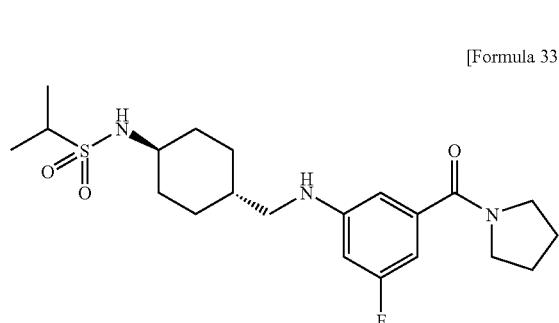
35

[Formula 340]



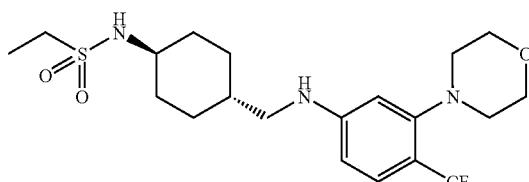
Compound II-173

Compound II-169



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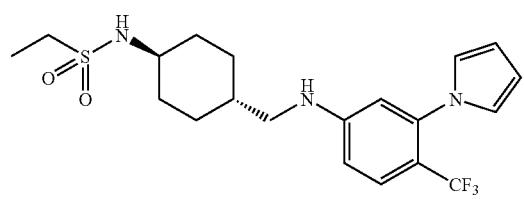
[Formula 341]



¹H-NMR (DMSO-d₆) δ: 0.95-1.08 (m, 2H), 1.15-1.28 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.43 (m, 1H), 1.76-1.85 (m, 2H), 1.85-1.93 (m, 2H), 2.76-2.82 (m, 2H), 2.88 (t, 2H, J=6.0 Hz), 2.97 (t, 2H, J=7.2 Hz), 3.00 (m, 1H), 3.64-3.70 (m, 4H), 6.33 (m, 1H), 6.37 (d, 1H, J=8.4 Hz), 6.56 (s, 1H), 7.00 (d, 1H, J=7.8 Hz), 7.28 (d, 1H, J=8.4 Hz).

407

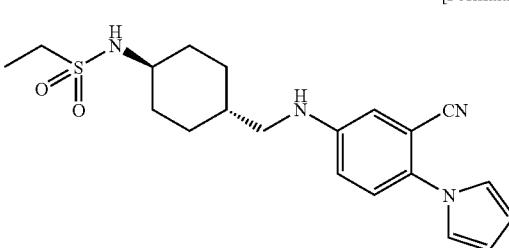
Compound II-174



[Formula 342]

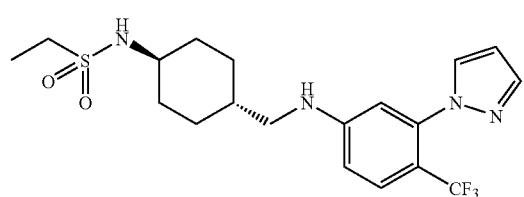
408

Compound II-179



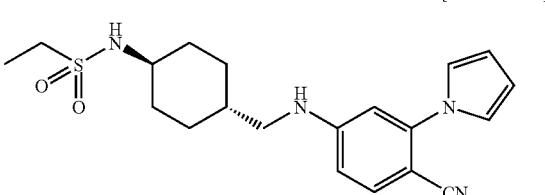
[Formula 347]

Compound II-175



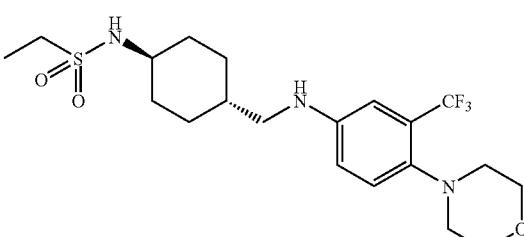
[Formula 343]

15 Compound II-180



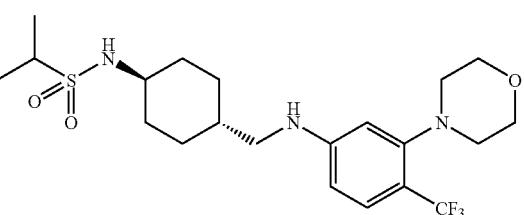
[Formula 348]

Compound II-176



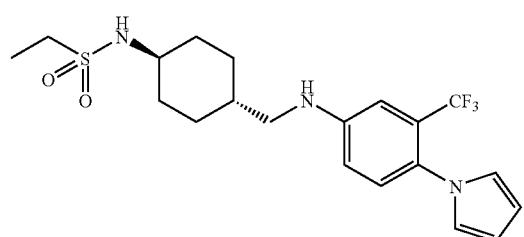
[Formula 344] 25

Compound II-181



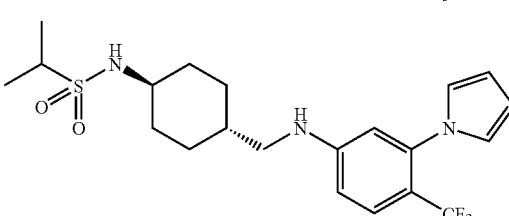
[Formula 349]

Compound II-177



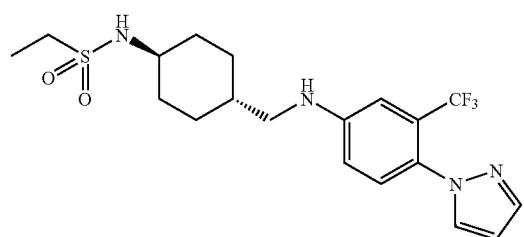
[Formula 345] 40

Compound II-182



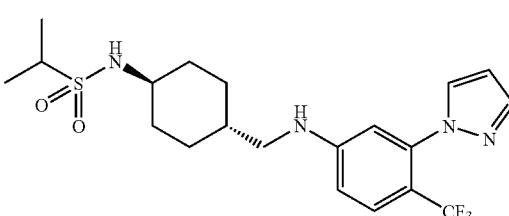
[Formula 350]

Compound II-178



[Formula 346]

55 Compound II-183



[Formula 351]

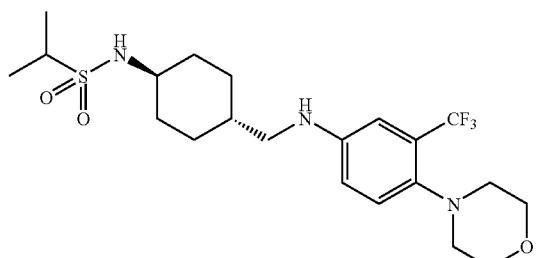
409

Compound II-184

410

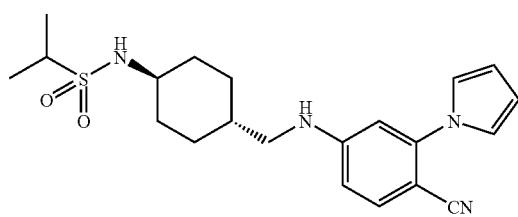
Compound II-188

[Formula 352] 5



Compound II-189

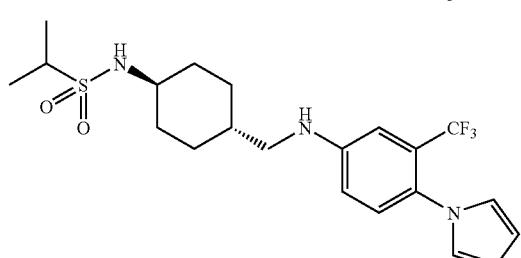
[Formula 356]



Compound II-185

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[Formula 353]



[Formula 357]



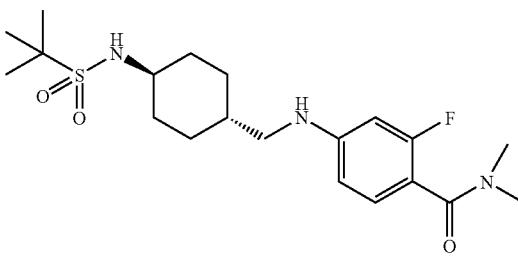
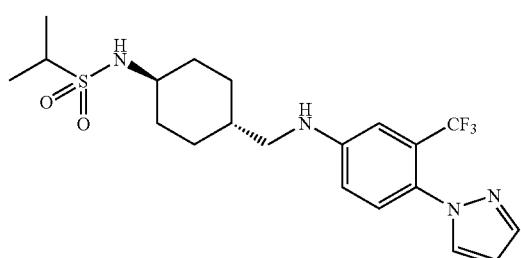
Compound II-190

Compound II-186

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[Formula 358]

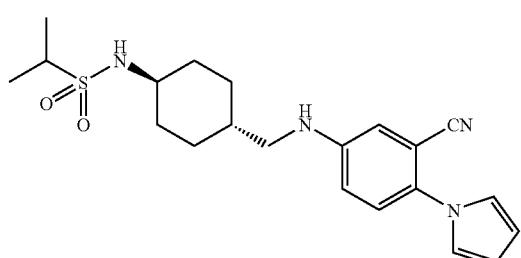
[Formula 354]



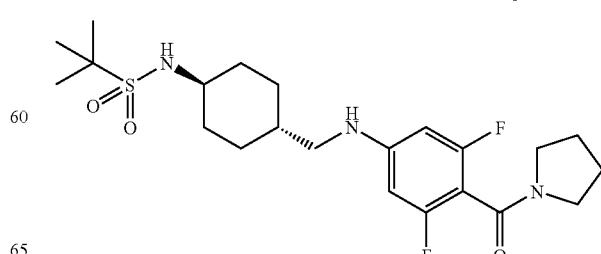
Compound II-187

Compound II-191

[Formula 355] 55

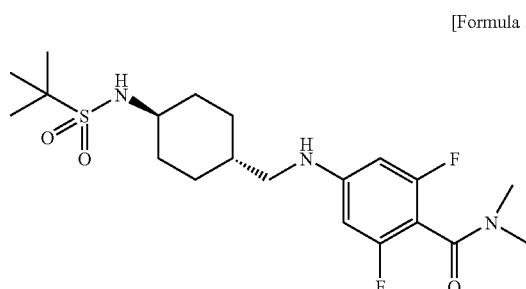


[Formula 359]

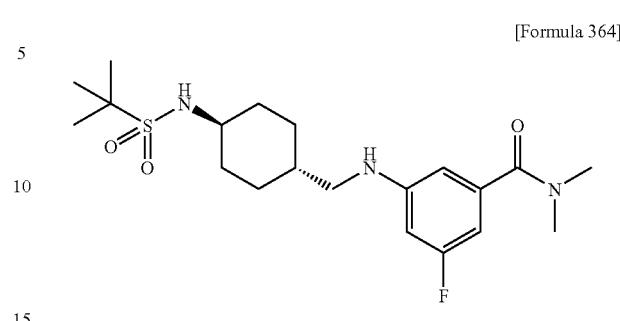


411

Compound II-192

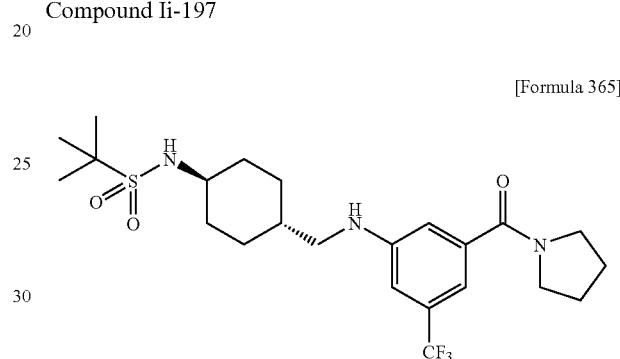
**412**

Compound II-196



Compound II-193

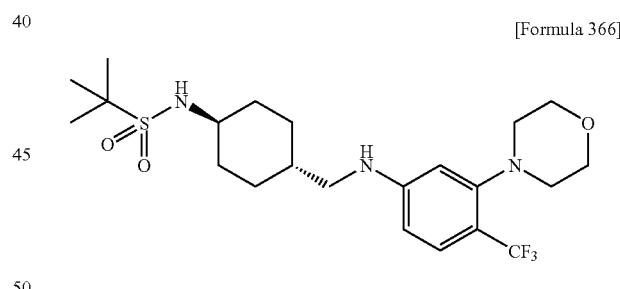
Compound II-197



Compound II-194

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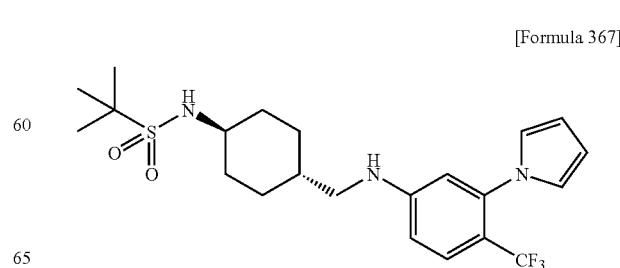
Compound II-198



Compound II-195

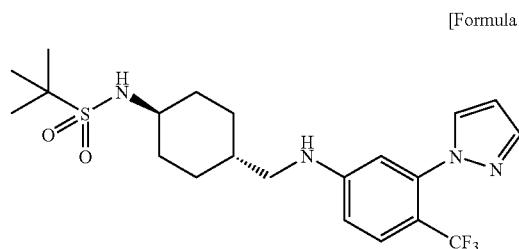
Compound II-199

[Formula 363]



413

Compound II-200



Compound II-201

[Formula 368]

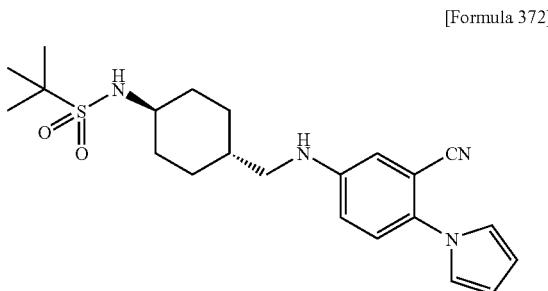
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414

Compound II-204



[Formula 372]

[Formula 368]

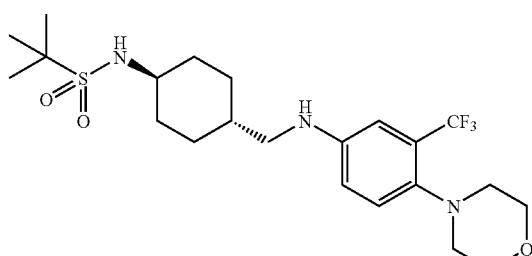
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Compound II-205

[Formula 369]



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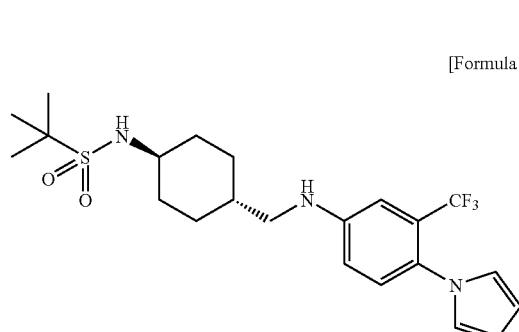
25

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Compound II-206

[Formula 373]

Compound II-202

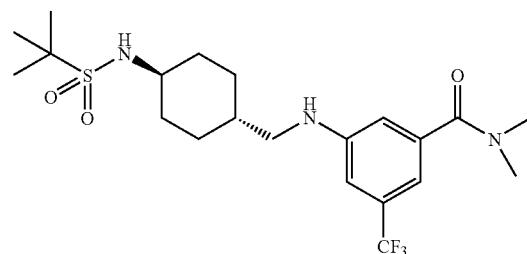


[Formula 370]

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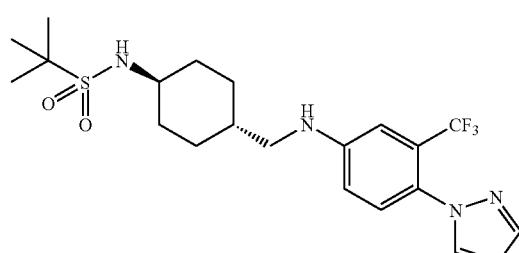
45



[Formula 374]

Compound Ij-2

Compound II-203

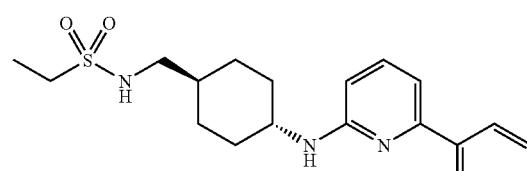


[Formula 371]

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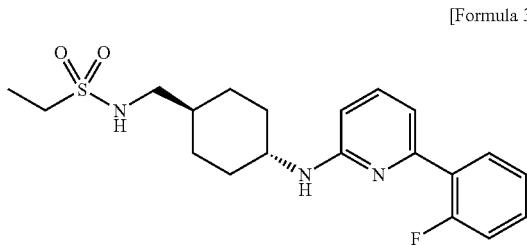


[Formula 375]

¹H-NMR (DMSO-d₆) δ: 0.98-1.24 (m, 4H), 1.19 (t, 3H, J=7.5 Hz), 1.40 (m, 1H), 1.78-1.88 (m, 2H), 2.02-2.14 (m, 2H), 2.80 (t, 2H, J=6.0 Hz), 2.86 (q, 2H, J=7.2 Hz), 3.64-3.82 (m, 1H), 6.40 (d, 2H, J=8.1 Hz), 7.01 (d, 2H, J=7.2 Hz), 7.32-7.50 (m, 4H), 7.99 (d, 2H, J=6.9 Hz)

415

Compound Ij-3



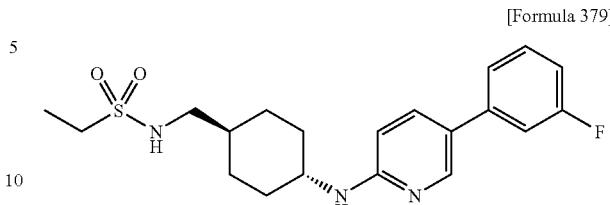
[Formula 376]

¹H-NMR (DMSO-d₆) δ: 0.96-1.26 (m, 4H), 1.18 (t, 3H, J=7.5 Hz), 1.40 (m, 1H), 1.78-1.88 (m, 2H), 2.02-2.14 (m, 2H), 2.78 (t, 2H, J=6.0 Hz), 2.98 (q, 2H, J=7.5 Hz), 3.60-3.78 (m, 1H), 6.40-6.50 (m, 2H), 6.85-6.92 (m, 1H), 6.97-7.03 (m, 1H), 7.22-7.35 (m, 2H), 7.36-7.46 (m, 2H), 7.88-7.96 (m, 1H)

Compound Ij-4

416

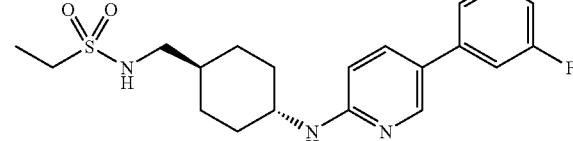
Compound Ij-6



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[Formula 379]

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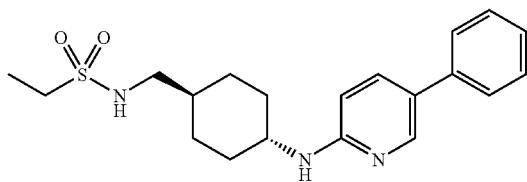
¹H-NMR (DMSO-d₆) δ: 0.92-1.24 (m, 4H), 1.19 (t, 3H, J=7.2 Hz), 1.40 (m, 1H), 1.78-1.88 (m, 2H), 1.96-2.06 (m, 2H), 2.78 (t, 2H, J=6.0 Hz), 2.98 (q, 2H, J=7.5 Hz), 3.60-3.78 (m, 1H), 6.51 (d, 1H, J=8.7 Hz), 6.60 (d, 1H, J=7.5 Hz), 7.01 (t, 1H, J=5.7 Hz), 7.02-7.12 (m, 1H), 7.36-7.48 (m, 3H), 7.71 (dd, 1H, J=8.7, 2.1 Hz), 8.33 (d, 1H, J=2.1 Hz)

Compound Ij-7

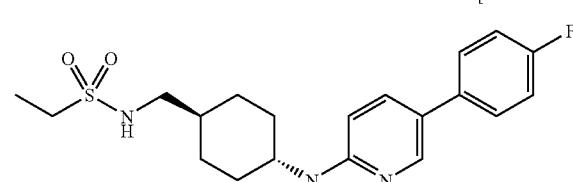
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[Formula 380]

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¹H-NMR (DMSO-d₆) δ: 0.92-1.24 (m, 4H), 1.19 (t, 3H, J=7.2 Hz), 1.38 (m, 1H), 1.78-1.88 (m, 2H), 1.96-2.06 (m, 2H), 2.78 (t, 2H, J=6.0 Hz), 2.98 (q, 2H, J=7.5 Hz), 3.60-3.78 (m, 1H), 6.50 (t, 1H, J=3.9 Hz), 6.53 (s, 1H), 7.00 (t, 1H, J=5.7 Hz), 7.25 (t, 1H, J=7.2 Hz), 7.34-7.45 (m, 2H), 7.55 (d, 2H, J=7.2 Hz), 7.67 (dd, 1H, J=8.7, 2.7 Hz), 8.29 (d, 1H, J=2.7 Hz)

Hz)

Compound Ij-5

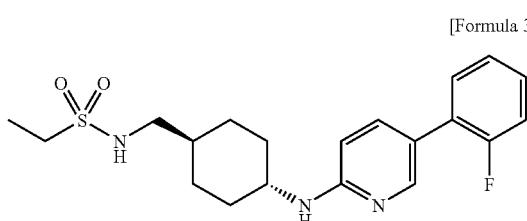
¹H-NMR (DMSO-d₆) δ: 0.92-1.24 (m, 4H), 1.19 (t, 3H, J=7.2 Hz), 1.40 (m, 1H), 1.78-1.88 (m, 2H), 1.96-2.06 (m, 2H), 2.78 (t, 2H, J=6.0 Hz), 2.98 (q, 2H, J=7.5 Hz), 3.60-3.78 (m, 1H), 6.50 (d, 2H, J=8.7 Hz), 6.99 (t, 1H, J=6.0 Hz), 7.16-7.26 (m, 2H), 7.52-7.68 (m, 3H), 8.25 (s, 1H)

Compound Ij-8

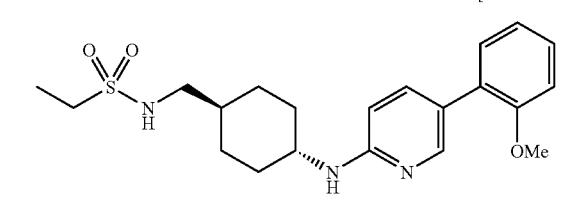
45

[Formula 381]

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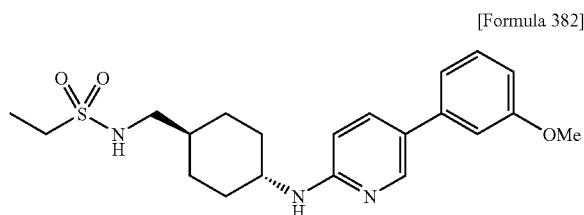
60

¹H-NMR (CDCl₃) δ: 1.15-1.26 (m, 4H), 1.40 (t, 3H, J=7.5 Hz), 1.55-1.58 (m, 1H), 1.93 (d, 2H, J=9.7 Hz), 2.23 (d, 2H, J=9.7 Hz), 3.01-3.11 (m, 4H), 3.56-3.61 (m, 1H), 3.84 (s, 3H), 4.34 (t, 1H, J=6.1 Hz), 4.83-4.86 (m, 1H), 6.46 (d, 1H, J=8.6 Hz), 6.99 (d, 1H, J=8.5 Hz), 7.05 (d, 1H, J=8.5 Hz), 7.29 (s, 1H), 7.30-7.34 (m, 1H), 7.69 (dd, 1H, J=8.7, 2.4 Hz), 8.25 (s, 1H).

¹H-NMR (DMSO-d₆) δ: 0.92-1.24 (m, 4H), 1.19 (t, 3H, J=7.2 Hz), 1.38 (m, 1H), 1.78-1.88 (m, 2H), 1.96-2.06 (m, 2H), 2.78 (t, 2H, J=6.0 Hz), 2.98 (q, 2H, J=7.5 Hz), 3.60-3.78 (m, 1H), 6.52 (d, 1H, J=8.4 Hz), 6.60 (d, 1H, J=7.8 Hz), 7.01 (t, 1H, J=5.7 Hz), 7.20-7.36 (m, 3H), 7.46 (t, 1H, J=8.1 Hz), 7.55 (d, 1H, J=8.7 Hz), 8.15 (s, 1H)

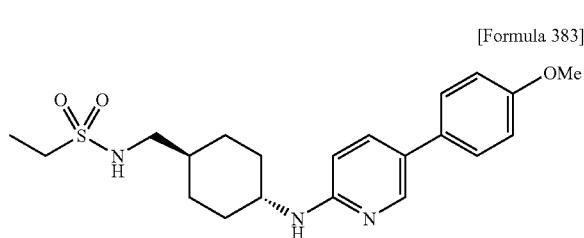
417

Compound Ij-9



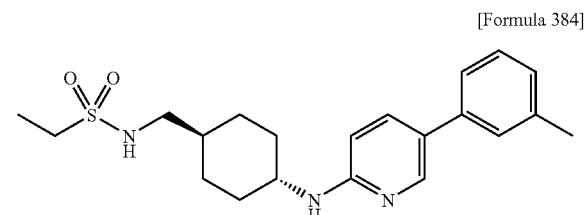
¹H-NMR (CDCl₃) δ: 1.16-1.24 (m, 4H), 1.40 (t, 3H, J=6.2 Hz), 1.55-1.59 (m, 1H), 1.94 (d, 2H, J=11.8 Hz), 2.23 (d, 2H, J=11.8 Hz), 3.03-3.09 (m, 4H), 3.58-3.62 (m, 1H), 3.88 (s, 3H), 4.29 (t, 1H, J=6.4 Hz), 4.85-4.89 (m, 1H), 6.49 (d, 1H, J=8.7 Hz), 6.88 (dd, 1H, J=8.7, 2.2 Hz), 7.04-7.06 (m, 1H), 7.10 (d, 1H, J=8.7 Hz), 7.36 (t, 1H, J=7.9 Hz), 7.70 (dd, 1H, J=8.7, 2.2 Hz), 8.32 (s, 1H).

Compound Ij-10



¹H-NMR (CDCl₃) δ: 1.19-1.30 (m, 4H), 1.41 (t, 3H, J=6.3 Hz), 1.56-1.59 (m, 1H), 1.94 (d, 2H, J=11.1 Hz), 2.23 (d, 2H, J=11.1 Hz), 3.01-3.11 (m, 4H), 3.57-3.61 (m, 1H), 3.87 (s, 3H), 4.27 (t, 1H, J=6.4 Hz), 4.98 (s, 1H), 6.50 (dd, 1H, J=8.7, 2.2 Hz), 6.99 (d, 2H, J=8.9 Hz), 7.43 (d, 2H, J=8.7 Hz), 7.68 (dd, 1H, J=8.7, 2.2 Hz), 8.25 (s, 1H).

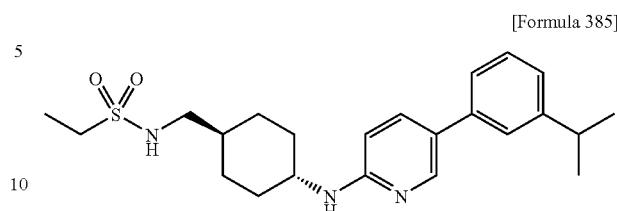
Compound Ij-11



¹H-NMR (DMSO-d₆) δ: 0.93-1.08 (m, 2H), 1.09-1.25 (m, 5H), 1.39 (m, 1H), 1.75-1.86 (m, 2H), 1.95-2.07 (m, 2H), 2.34 (s, 3H), 2.78 (t, 2H, J=6.2 Hz), 2.98 (q, 2H, J=7.3 Hz), 3.65 (m, 1H), 6.45-6.53 (m, 2H), 7.01 (t, 1H, J=5.6 Hz), 7.07 (d, 1H, J=7.1 Hz), 7.23-7.38 (m, 3H), 7.64 (dd, 1H, J₁=8.8 Hz, J₂=2.5 Hz), 8.26 (d, 1H, J=2.5 Hz).

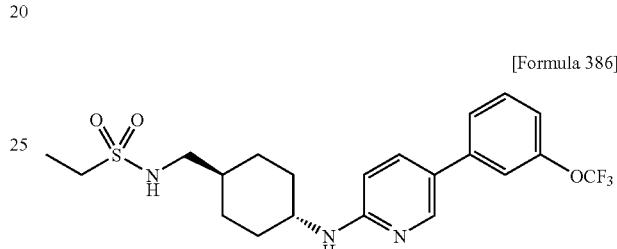
418

Compound Ij-12



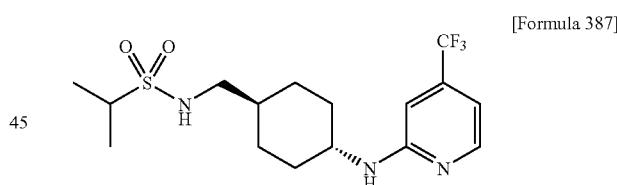
¹H-NMR (DMSO-d₆) δ: 0.93-1.08 (m, 2H), 1.09-1.27 (m, 11H), 1.39 (m, 1H), 1.76-1.87 (m, 2H), 1.96-2.06 (m, 2H), 2.78 (t, 2H, J=6.2 Hz), 2.84-3.03 (m, 3H), 3.66 (m, 1H), 6.45-6.54 (m, 2H), 7.01 (t, 1H, J=5.8 Hz), 7.13 (d, 1H, J=6.9 Hz), 7.27-7.41 (m, 3H), 7.66 (dd, 1H, J₁=8.8 Hz, J₂=2.5 Hz), 8.27 (d, 1H, J=2.2 Hz).

Compound Ij-13



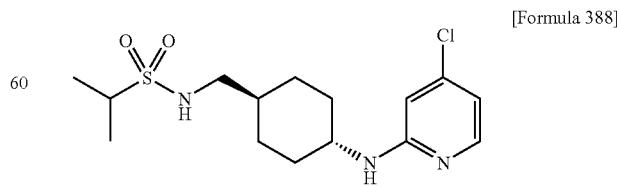
¹H-NMR (DMSO-d₆) δ: 0.92-1.09 (m, 2H), 1.09-1.25 (m, 5H), 1.39 (m, 1H), 1.76-1.85 (m, 2H), 1.95-2.06 (m, 2H), 2.78 (t, 2H, J=6.2 Hz), 2.98 (q, 2H, J=7.3 Hz), 3.68 (m, 1H), 6.52 (d, 1H, J=8.8 Hz), 6.66 (d, 1H, J=8.0 Hz), 7.02 (t, 1H, J=5.5 Hz), 7.23 (d, 1H, J=8.1 Hz), 7.49-7.55 (m, 2H), 7.62 (d, 1H, J₁=8.5 Hz), 7.72 (dd, 1H, J₁=8.8 Hz, J₂=2.5 Hz), 8.35 (d, 1H, J=2.5 Hz).

Compound Ij-14



¹H-NMR (DMSO-d₆) δ: 0.92-1.22 (m, 4H), 1.22 (d, 6H, J=6.4 Hz), 1.39 (m, 1H), 1.76-1.86 (m, 2H), 1.95-2.03 (m, 2H), 2.81 (t, 2H, J=6.4 Hz), 3.10-3.20 (m, 1H), 3.60-3.75 (m, 1H), 6.65 (d, 1H, J=4.8 Hz), 6.70 (s, 1H), 6.88-6.98 (m, 2H), 8.16 (d, 1H, J=5.2 Hz).

Compound Ij-15

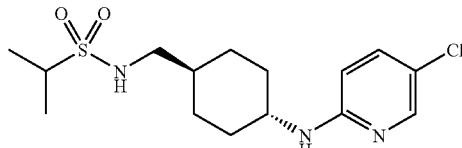


¹H-NMR (CDCl₃) δ: 1.02-1.28 (m, 4H), 1.38 (d, 6H, J=6.9 Hz), 1.52 (m, 1H), 1.85-1.94 (m, 2H), 2.11-2.21 (m, 2H), 3.01

419

(t, 2H, J=6.6 Hz), 3.10-3.25 (m, 1H), 3.38-3.54 (m, 1H), 4.22 (t, 1H, J=6.3 Hz), 4.58 (d, 1H, J=7.8 Hz), 6.34 (d, 1H, J=1.8 Hz), 6.53 (dd, 1H, J=5.4, 1.8 Hz), 7.93 (d, 1H, J=5.4 Hz).

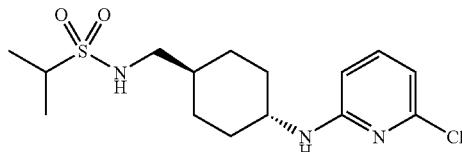
Compound Ij-16



[Formula 389]

¹H-NMR (CDCl₃) δ: 1.03-1.28 (m, 4H), 1.37 (d, 6H, J=6.9 Hz), 1.52 (m, 1H), 1.84-1.93 (m, 2H), 2.11-2.21 (m, 2H), 3.01 (t, 2H, J=6.6 Hz), 3.09-3.24 (m, 1H), 3.40-3.54 (m, 1H), 4.26 (t, 1H, J=6.6 Hz), 4.44 (d, 1H, J=8.1 Hz), 6.29 (d, 1H, J=8.7 Hz), 7.33 (dd, 1H, J=8.7, 2.7 Hz), 7.99 (d, 1H, J=2.7 Hz).

Compound Ij-17

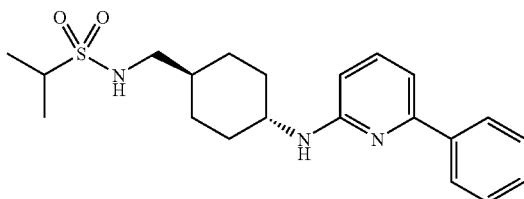


[Formula 390]

¹H-NMR (DMSO-d₆) δ: 0.92-1.22 (m, 4H), 1.21 (d, 6H, J=6.8 Hz), 1.36 (m, 1H), 1.76-1.84 (m, 2H), 1.92-2.00 (m, 2H), 2.80 (t, 2H, J=6.4 Hz), 3.08-3.18 (m, 1H), 3.45-3.56 (m, 1H), 6.36 (d, 1H, J=8.4 Hz), 6.43 (d, 1H, J=7.2 Hz), 6.75 (d, 1H, J=7.6 Hz), 6.94 (t, 1H, J=6.0 Hz), 7.33 (t, 1H, J=7.6 Hz).

Compound Ij-18

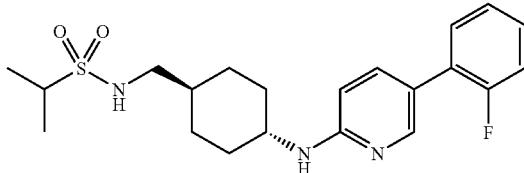
[Formula 391]



¹H-NMR (DMSO-d₆) δ: 0.98-1.24 (m, 4H), 1.22 (d, 6H, J=6.9 Hz), 1.40 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.14 (m, 2H), 2.83 (t, 2H, J=6.0 Hz), 3.10-3.22 (m, 1H), 3.64-3.82 (m, 1H), 6.40 (d, 2H, J=8.4 Hz), 6.95-7.05 (m, 2H), 7.35-7.50 (m, 4H), 7.99 (d, 2H, J=7.2 Hz)

Compound Ij-19

[Formula 392]

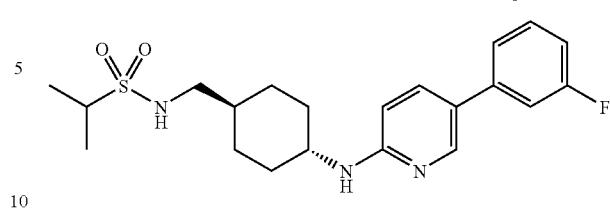


¹H-NMR (CDCl₃) δ: 1.22-1.38 (m, 4H), 1.38 (d, 6H, J=8.0 Hz), 1.54 (m, 1H), 1.86-1.95 (m, 2H), 2.18-2.26 (m, 2H), 3.03 (t, 2H, J=6.0 Hz), 3.12-3.22 (m, 1H), 3.52-3.64 (m, 1H), 4.16 (t, 1H, J=6.4 Hz), 4.82-4.92 (m, 1H), 6.46 (d, 1H, J=8.0 Hz), 7.10-7.20 (m, 2H), 7.23-7.33 (m, 1H), 7.37 (t, 1H, J=8.0 Hz), 7.65 (d, 1H, J=8.7 Hz), 8.24 (s, 1H).

420

Compound Ij-20

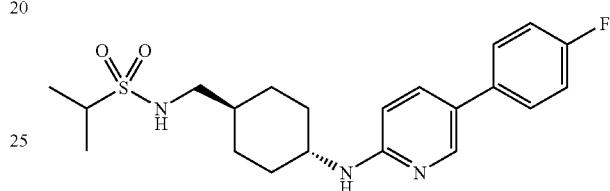
[Formula 393]



10

¹H-NMR (CDCl₃) δ: 1.22-1.38 (m, 4H), 1.39 (d, 6H, J=8.0 Hz), 1.54 (m, 1H), 1.86-1.95 (m, 2H), 2.18-2.26 (m, 2H), 3.03 (t, 2H, J=6.0 Hz), 3.12-3.22 (m, 1H), 3.52-3.64 (m, 1H), 4.16 (t, 1H, J=6.4 Hz), 4.78-4.88 (m, 1H), 6.46 (d, 1H, J=8.0 Hz), 6.98 (t, 1H, J=5.7 Hz), 7.18 (d, 1H, J=8.0 Hz), 7.23-7.29 (m, 11H), 7.33-7.40 (m, 1H), 7.65 (d, 1H, J=8.7 Hz), 8.29 (s, 1H). Compound Ij-21

[Formula 394]

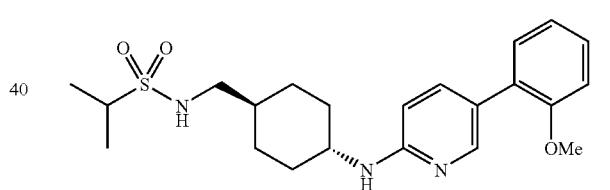


20

¹H-NMR (CDCl₃) δ: 1.10-1.30 (m, 4H), 1.38 (d, 6H, J=8.0 Hz), 1.54 (m, 1H), 1.86-1.95 (m, 2H), 2.18-2.26 (m, 2H), 3.03 (t, 2H, J=6.0 Hz), 3.13-3.22 (m, 1H), 3.52-3.64 (m, 1H), 4.15 (t, 1H, J=6.4 Hz), 4.78-4.88 (m, 1H), 6.46 (d, 1H, J=8.0 Hz), 7.07-7.14 (m, 2H), 7.40-7.46 (m, 2H), 7.62 (d, 1H, J=8.7 Hz), 8.23 (s, 1H).

35 Compound Ij-22

[Formula 395]

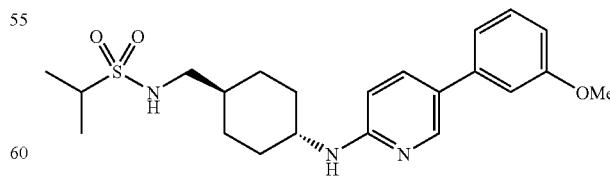


45

¹H-NMR (DMSO-d₆) δ: 0.95-1.25 (m, 4H), 1.22 (d, 6H, J=6.6 Hz), 1.25-1.50 (br, 1H), 1.81 (d, 2H, J=11.4 Hz), 2.00 (d, 2H, J=10.5 Hz), 2.81 (t, 2H, J=6.6 Hz), 3.05-3.22 (m, 1H), 3.58-3.80 (m, 1H), 3.76 (s, 3H), 6.49 (d, 2H, J=8.7 Hz), 6.50-6.70 (br, 1H), 6.95-7.10 (m, 3H), 7.20-7.32 (m, 2H), 7.51 (d, 1H, J=7.2 Hz), 8.05 (br, 1H). ESI(positive) 418.3 [M+H]⁺ Compound Ij-23

55 Compound Ij-23

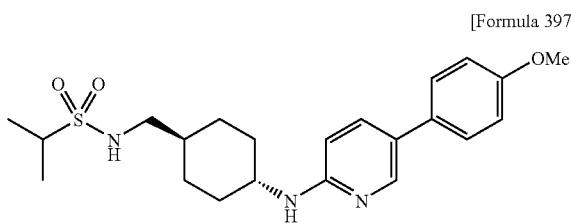
[Formula 396]



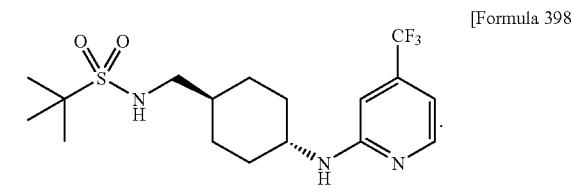
¹H-NMR (DMSO-d₆) δ: 0.95-1.32 (m, 4H), 1.22 (d, 6H, J=6.6 Hz), 1.25-1.55 (br, 1H), 1.82 (d, 2H, J=11.4 Hz), 2.01 (d, 2H, J=10.2 Hz), 2.81 (t, 2H, J=6.6 Hz), 3.05-3.22 (m, 1H), 3.58-3.78 (m, 1H), 3.80 (s, 3H), 6.59 (d, 2H, J=9.6 Hz), 6.85 (dd, 1H, J=8.4 Hz, 2.4 Hz), 6.99 (t, 3H, J=5.7 Hz), 7.05-7.18

421

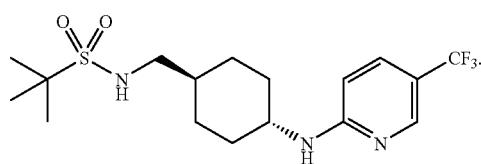
(m, 2H), 7.32 (d, 1H, $J=7.8$ Hz), 7.76 (d, 1H, $J=8.4$ Hz), 8.27 (d, 1H, $J=2.1$ Hz). ESI(positive) 418.3 [M+H]⁺
Compound Ij-24



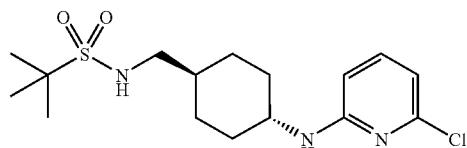
1H-NMR (DMSO-d6) δ: 0.92-1.25 (m, 4H), 1.22 (d, 6H, $J=6.6$ Hz), 1.28-1.48 (m, 11H), 1.81 (d, 2H, $J=10.8$ Hz), 2.00 (d, 2H, $J=9.6$ Hz), 2.81 (t, 2H, $J=6.6$ Hz), 3.08-3.22 (m, 1H), 3.58-3.74 (m, 1H), 3.77 (s, 3H), 6.51 (d, 2H, $J=8.7$ Hz), 6.97 (d, 2H, $J=8.7$ Hz), 6.98 (brs, 1H), 7.48 (d, 2H, $J=8.7$ Hz), 7.63 (dd, 1H, $J=11.4$ Hz, 2.4 Hz), 8.21 (d, 1H, $J=2.4$ Hz). ESI (positive) 418.3[M+H]⁺
Compound Ij-25



1H-NMR (DMSO-d6) δ: 0.92-1.22 (m, 4H), 1.27 (s, 9H), 1.38 (m, 1H), 1.78-1.88 (m, 2H), 1.95-2.05 (m, 2H), 2.88 (t, 2H, $J=6.0$ Hz), 3.60-3.80 (m, 11H), 6.65 (d, 1H, $J=5.4$ Hz), 6.70 (s, 1H), 6.87 (t, 1H, $J=6.0$ Hz), 6.94 (d, 1H, $J=7.8$ Hz), 8.16 (d, 1H, $J=5.4$ Hz)
Compound Ij-26

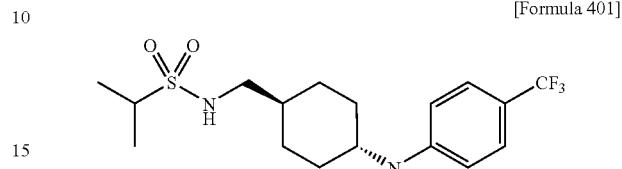


1H-NMR (DMSO-d6) δ: 0.92-1.22 (m, 4H), 1.27 (s, 9H), 1.38 (m, 1H), 1.78-1.88 (m, 2H), 1.94-2.04 (m, 2H), 2.88 (t, 2H, $J=6.0$ Hz), 3.60-3.80 (m, 1H), 6.53 (d, 1H, $J=8.7$ Hz), 6.87 (t, 1H, $J=5.7$ Hz), 7.19 (d, 1H, $J=7.5$ Hz), 7.59 (dd, 1H, $J=9.0$, 2.4 Hz), 8.26 (d, 1H, $J=2.4$ Hz)
Compound Ij-27

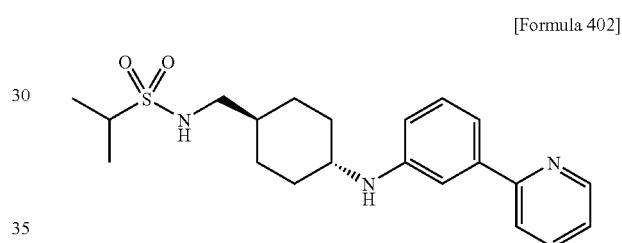
**422**

1H-NMR (DMSO-d6) δ: 0.92-1.22 (m, 4H), 1.26 (s, 9H), 1.38 (m, 1H), 1.76-1.86 (m, 2H), 1.92-2.02 (m, 2H), 2.88 (t, 2H, $J=6.0$ Hz), 3.40-3.60 (m, 1H), 6.36 (d, 1H, $J=8.1$ Hz), 6.43 (d, 1H, $J=6.9$ Hz), 6.80 (d, 1H, $J=7.5$ Hz), 6.86 (t, 1H, $J=5.4$ Hz), 7.34 (t, 1H, $J=8.4$ Hz)

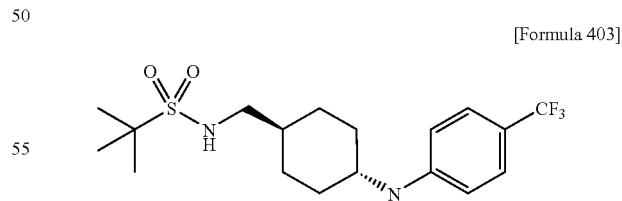
Compound Ij-28



1H-NMR ((DMSO-d6) δ: 0.93-1.18 (m, 4H), 1.21 (d, 6H, $J=6.9$ Hz), 1.39 (m, 1H), 1.75-1.86 (m, 2H), 1.94-2.05 (m, 2H), 2.80 (t, 2H, $J=6.0$ Hz), 3.09-3.27 (m, 2H), 6.19 (d, 1H, $J=8.1$ Hz), 6.64 (d, 2H, $J=8.7$ Hz), 6.98 (t, 1H, $J=6.0$ Hz), 7.33 (d, 2H, $J=8.7$ Hz) Mass: 379[M+H]⁺
Compound Ij-29



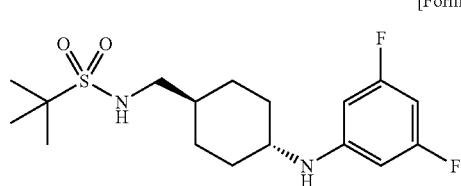
1H-NMR (DMSO-d6) δ: 0.93-1.18 (m, 4H), 1.22 (s, 3H), 1.24 (s, 3H), 1.32-1.49 (m, 2H), 1.82 (d, 2H, $J=11.2$ Hz), 2.04 (d, 2H, $J=11.2$ Hz), 2.75-2.87 (m, 2H), 3.07-3.28 (m, 2H), 6.64 (s, 11H), 6.96 (s, 1H), 7.10-7.22 (m, 2H), 7.25-7.39 (m, 2H), 7.77-7.90 (m, 2H), 8.63 (s, 1H). Melting point: 161 to 162°C.
Compound Ij-30



1H-NMR (DMSO-d6) δ: 0.92-1.22 (m, 4H), 1.27 (s, 9H), 1.37 (m, 1H), 1.76-1.86 (m, 2H), 1.94-2.05 (m, 2H), 2.88 (t, 2H, $J=6.3$ Hz), 3.19 (m, 1H), 6.19 (d, 1H, $J=7.5$ Hz), 6.64 (d, 2H, $J=8.7$ Hz), 6.88 (d, 1H, $J=6.0$ Hz), 7.33 (d, 2H, $J=8.7$ Hz)
Mass: 392M⁺

423

Compound Ij-31



[Formula 404]

¹H-NMR (DMSO-d₆) δ: 0.92-1.16 (m, 4H), 1.26 (s, 9H), 1.36 (m, 1H), 1.72-1.83 (m, 2H), 1.92-2.02 (m, 2H), 2.87 (t, 2H, J=6.3 Hz), 3.12 (m, 1H), 6.09-6.23 (m, 4H), 6.87 (t, 1H, J=6.0 Hz) Mass: 361[M+H]⁺

Compound Ij-32

¹H-NMR (CDCl₃) δ: 1.00-1.20 (m, 4H), 1.40 (s, 9H), 1.42-1.64 (m, 2H), 1.84-1.95 (m, 2H), 2.09-2.20 (m, 2H), 3.07 (m, 1H), 3.07 (t, 2H, J=6.3 Hz), 3.90 (m, 1H), 6.10 (dd, 2H, J=9.6, 5.4 Hz).

Compound Ij-33

¹H-NMR (DMSO-d₆) δ: 0.93-1.21 (m, 5H), 1.28 (s, 9H), 1.33-1.46 (m, 1H), 1.82 (d, 2H, J=11.6 Hz), 2.04 (d, 2H, J=11.6 Hz), 2.86-2.95 (m, 2H), 3.03-3.29 (m, 1H), 6.59-6.71 (m, 1H), 6.80-6.92 (m, 1H), 7.09-7.21 (m, 2H), 7.27-7.37 (m, 2H), 7.77-7.88 (m, 2H), 8.58-8.67 (s, 1H). Melting point: 172 to 173° C.

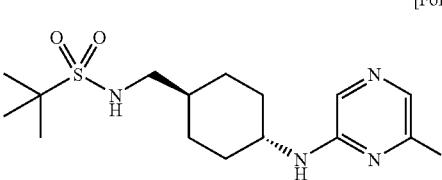
Compound Ij-34

¹H-NMR (DMSO-d₆) δ: 0.96-1.08 (m, 2H), 1.12-1.24 (m, 2H), 1.21 (d, 6H, J=6.4 Hz), 1.38 (m, 1H), 1.76-1.86 (m, 2H), 1.92-2.00 (m, 2H), 2.80 (t, 2H, J=6.4 Hz), 3.10-3.20 (m, 1H),

424

3.48-3.60 (m, 1H), 6.95 (t, 1H, J=5.6 Hz), 7.41 (d, 1H, J=7.6 Hz), 7.63 (s, 1H), 7.82 (s, 1H).

Compound Ij-35

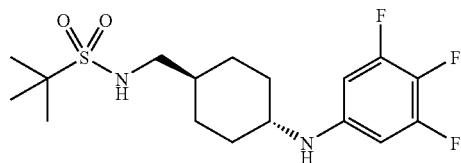


[Formula 408]

¹H-NMR (DMSO-d₆) δ: 0.96-1.26 (m, 4H), 1.27 (s, 9H), 1.38 (m, 1H), 1.78-1.88 (m, 2H), 1.92-2.02 (m, 2H), 2.88 (t, 2H, J=6.0 Hz), 3.48-3.62 (m, 1H), 6.87 (t, 1H, J=6.0 Hz), 7.45 (d, 1H, J=7.5 Hz), 7.63 (s, 1H), 7.82 (s, 1H)

Compound Ij-36

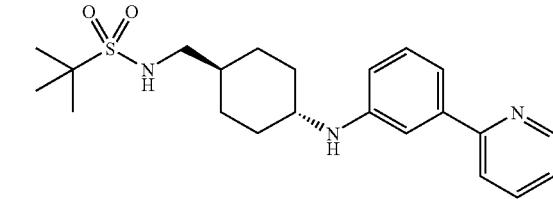
[Formula 405]



¹H-NMR (CDCl₃) δ: 1.00-1.20 (m, 4H), 1.40 (s, 9H), 1.42-1.64 (m, 2H), 1.84-1.95 (m, 2H), 2.09-2.20 (m, 2H), 3.07 (m, 1H), 3.07 (t, 2H, J=6.3 Hz), 3.90 (m, 1H), 6.10 (dd, 2H, J=9.6, 5.4 Hz).

Compound Ij-33

[Formula 406]



[Formula 409]

¹H-NMR (DMSO-d₆) δ: 0.96-1.06 (m, 2H), 1.12-1.20 (m, 2H), 1.21 (d, 6H, J=6.6 Hz), 1.39 (m, 1H), 1.78-1.84 (m, 2H), 1.95-1.99 (m, 2H), 2.81 (t, 2H, J=6.0 Hz), 3.10-3.20 (m, 1H), 3.74-3.88 (m, 1H), 6.80 (s, 1H), 6.98 (t, 1H, J=6.0 Hz), 7.93 (d, 2H, J=7.2 Hz), 8.53 (s, 1H).

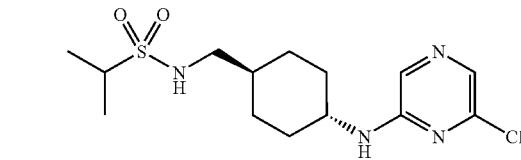
Compound Ij-37

[Formula 407]

¹H-NMR (DMSO-d₆) δ: 0.93-1.21 (m, 5H), 1.28 (s, 9H), 1.33-1.46 (m, 1H), 1.82 (d, 2H, J=11.6 Hz), 2.04 (d, 2H, J=11.6 Hz), 2.86-2.95 (m, 2H), 3.03-3.29 (m, 1H), 6.59-6.71 (m, 1H), 6.80-6.92 (m, 1H), 7.09-7.21 (m, 2H), 7.27-7.37 (m, 2H), 7.77-7.88 (m, 2H), 8.58-8.67 (s, 1H). Melting point: 172 to 173° C.

Compound Ij-34

[Formula 408]



[Formula 410]

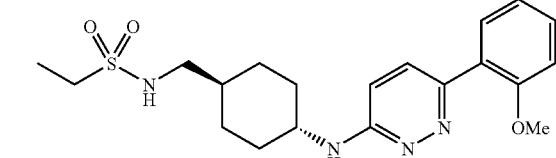
¹H-NMR (DMSO-d₆) δ: 0.96-1.30 (m, 4H), 1.19 (t, 3H, J=7.2 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.80 (t, 2H, J=6.0 Hz), 2.99 (q, 2H, J=7.5 Hz), 3.72-3.90 (m, 1H), 6.85 (d, 1H, J=9.6 Hz), 6.93 (d, 1H, J=7.5 Hz), 7.04 (t, 1H, J=5.7 Hz), 7.26-7.38 (m, 2H), 7.40-7.52 (m, 1H), 7.57 (d, 1H, J=9.0 Hz), 7.85 (t, 1H, J=7.8 Hz)

Compound Ij-38

[Formula 409]

¹H-NMR (DMSO-d₆) δ: 0.96-1.08 (m, 2H), 1.12-1.24 (m, 2H), 1.21 (d, 6H, J=6.4 Hz), 1.38 (m, 1H), 1.76-1.86 (m, 2H), 1.92-2.00 (m, 2H), 2.80 (t, 2H, J=6.4 Hz), 3.10-3.20 (m, 1H),

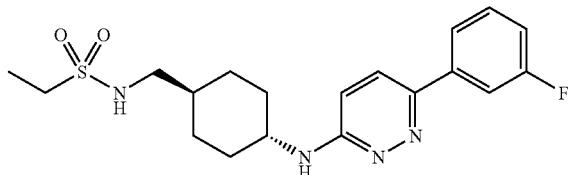
[Formula 411]



425

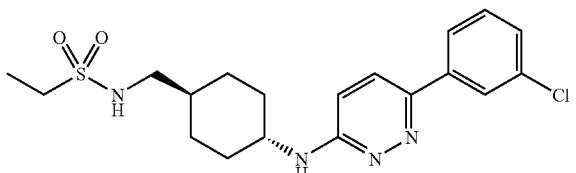
¹H-NMR (DMSO-d₆) δ: 0.96-1.30 (m, 4H), 1.19 (t, 3H, J=7.2 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.80 (t, 2H, J=6.0 Hz), 2.99 (q, 2H, J=7.5 Hz), 3.72-3.90 (m, 1H), 3.80 (s, 3H), 6.72 (d, 1H, J=7.8 Hz), 6.77 (d, 1H, J=9.0 Hz), 6.98-7.10 (m, 2H), 7.12 (d, 1H, J=8.4 Hz), 7.38 (t, 1H, J=8.1 Hz), 7.56 (d, 1H, J=9.3 Hz), 7.61 (d, 1H, J=7.8 Hz)

Compound Ij-39



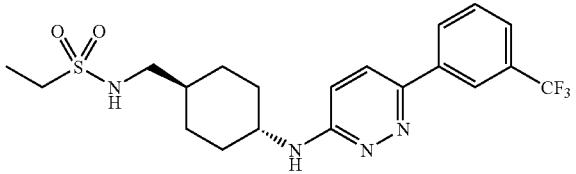
¹H-NMR (DMSO-d₆) δ: 0.96-1.30 (m, 4H), 1.19 (t, 3H, J=7.2 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.80 (t, 2H, J=6.3 Hz), 2.99 (q, 2H, J=7.5 Hz), 3.72-3.90 (m, 1H), 6.85 (d, 1H, J=9.6 Hz), 6.92 (d, 1H, J=7.5 Hz), 7.04 (t, 1H, J=5.7 Hz), 7.21 (t, 1H, J=8.7 Hz), 7.46-7.56 (m, 1H), 7.75-7.88 (m, 3H)

Compound Ij-40



¹H-NMR (DMSO-d₆) δ: 0.96-1.10 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.15-1.26 (m, 2H), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.14 (m, 2H), 2.80 (t, 2H, J=6.3 Hz), 2.99 (q, 2H, J=7.5 Hz), 3.76-3.87 (m, 1H), 6.85 (d, 1H, J=9.6 Hz), 6.91 (d, 1H, J=7.5 Hz), 7.01 (t, 1H, J=5.7 Hz), 7.42-7.52 (m, 2H), 7.83 (d, 1H, J=8.0 Hz), 7.93 (d, 1H, J=8.0 Hz), 8.02 (s, 1H).

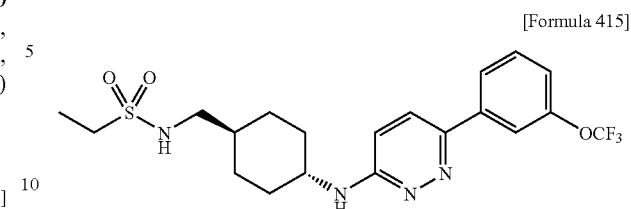
Compound Ij-41



¹H-NMR (DMSO-d₆) δ: 0.96-1.30 (m, 4H), 1.20 (t, 3H, J=7.5 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.80 (t, 2H, J=6.3 Hz), 2.99 (q, 2H, J=7.5 Hz), 3.76-3.90 (m, 1H), 6.88 (d, 1H, J=9.3 Hz), 6.97 (d, 1H, J=7.5 Hz), 7.03 (t, 1H, J=5.7 Hz), 7.67-7.77 (m, 2H), 7.92 (d, 1H, J=9.6 Hz), 8.26 (d, 1H, J=6.9 Hz), 8.33 (s, 1H)

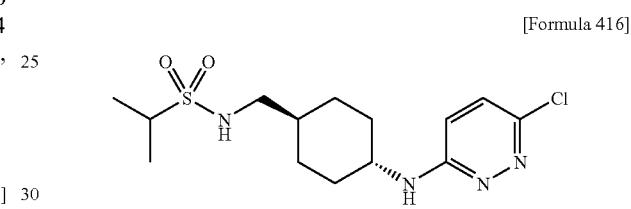
426

Compound Ij-42



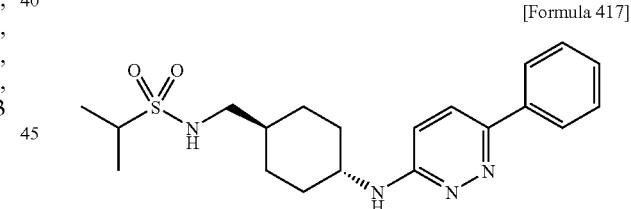
¹H-NMR (DMSO-d₆) δ: 0.93-1.10 (m, 2H), 1.20 (t, 3H, J=7.2 Hz), 1.22-1.28 (m, 1H), 1.35-1.50 (m, 2H), 1.84 (d, 2H, J=12.0 Hz), 2.08 (d, 2H, J=12.0 Hz), 2.63-2.76 (m, 2H), 2.91-3.03 (m, 2H), 3.75-3.90 (m, 1H), 6.86 (d, 1H, J=9.2 Hz), 6.93 (d, 1H, J=7.2 Hz), 6.98-7.07 (m, 1H), 7.36 (d, 1H, J=7.2 Hz), 7.59 (t, 1H, J=8.0 Hz), 7.85 (d, 1H, J=9.2 Hz), 7.91-8.02 (m, 2H). Melting point: 144 to 145°C.

Compound Ij-43



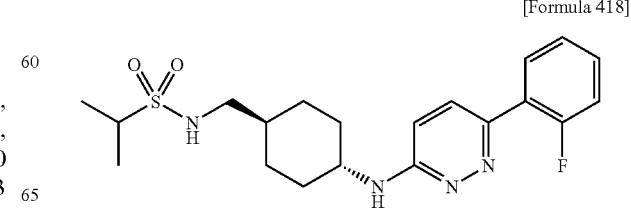
¹H-NMR (DMSO-d₆) δ: 0.94-1.06 (m, 2H), 1.10-1.24 (m, 2H), 1.21 (d, 6H, J=6.8 Hz), 1.39 (m, 1H), 1.76-1.86 (m, 2H), 1.98-2.06 (m, 2H), 2.81 (t, 2H, J=6.4 Hz), 3.10-3.20 (m, 1H), 3.62-3.74 (m, 1H), 6.84 (d, 1H, J=9.2 Hz), 6.88-6.98 (m, 2H), 7.31 (d, 1H, J=9.6 Hz).

Compound Ij-44



¹H-NMR (DMSO-d₆) δ: 0.94-1.26 (m, 4H), 1.20 (d, 6H, J=6.6 Hz), 1.40 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.81 (t, 2H, J=6.3 Hz), 3.06-3.20 (m, 1H), 3.72-3.90 (m, 1H), 6.75-6.88 (m, 2H), 6.97 (t, 1H, J=6.0 Hz), 7.30-7.48 (m, 3H), 7.76 (d, 1H, J=9.3 Hz), 7.94 (d, 2H, J=8.4 Hz)

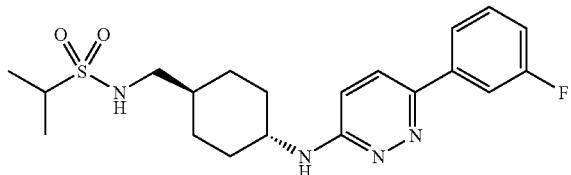
Compound Ij-45



427

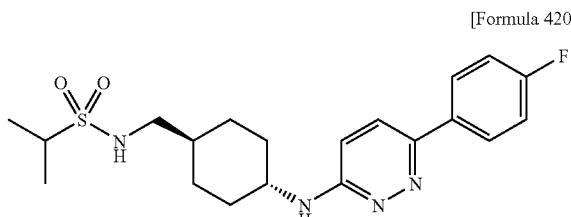
1H-NMR (DMSO-d₆) δ: 0.96-1.28 (m, 4H), 1.22 (d, 6H, J=6.9 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.83 (t, 2H, J=6.3 Hz), 3.10-3.22 (m, 1H), 3.74-3.92 (m, 1H), 6.85 (d, 1H, J=9.0 Hz), 6.91 (d, 1H, J=7.5 Hz), 6.98 (t, 1H, J=6.0 Hz), 7.25-7.36 (m, 2H), 7.40-7.50 (m, 1H), 7.57 (d, 1H, J=6.9 Hz), 7.85 (t, 1H, J=8.1 Hz)

Compound Ij-46



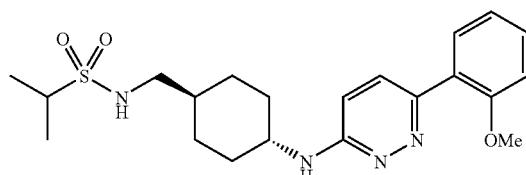
1H-NMR (DMSO-d₆) δ: 0.96-1.28 (m, 4H), 1.22 (d, 6H, J=6.6 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.83 (t, 2H, J=6.3 Hz), 3.10-3.22 (m, 1H), 3.74-3.92 (m, 1H), 6.85 (d, 1H, J=9.3 Hz), 6.90 (d, 1H, J=7.5 Hz), 6.98 (t, 1H, J=6.0 Hz), 7.21 (t, 1H, J=7.8 Hz), 7.46-7.56 (m, 1H), 7.75-7.86 (m, 3H)

Compound Ij-47



1H-NMR (DMSO-d₆) δ: 0.96-1.28 (m, 4H), 1.22 (d, 6H, J=6.9 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.83 (t, 2H, J=6.0 Hz), 3.10-3.22 (m, 1H), 3.74-3.92 (m, 1H), 6.81 (d, 1H, J=7.5 Hz), 6.84 (d, 1H, J=9.3 Hz), 6.98 (t, 1H, J=6.3 Hz), 7.25-7.35 (m, 2H), 7.77 (d, 1H, J=9.3 Hz), 7.96-8.06 (m, 2H)

Compound Ij-48



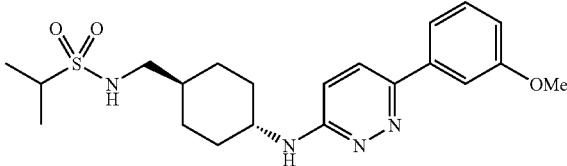
1H-NMR (DMSO-d₆) δ: 0.96-1.28 (m, 4H), 1.22 (d, 6H, J=6.9 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.83 (t, 2H, J=6.3 Hz), 3.10-3.22 (m, 1H), 3.74-3.92 (m, 1H), 3.80 (s, 3H), 6.71 (d, 1H, J=7.8 Hz), 6.76 (d, 1H, J=9.3 Hz), 6.98 (t, 1H, J=5.7 Hz), 7.05 (d, 1H, J=7.2 Hz), 7.12 (d, 1H, J=7.8 Hz), 7.38 (t, 1H, J=8.4 Hz), 7.56 (d, 1H, J=9.3 Hz), 7.62 (d, 1H, J=6.9 Hz)

428

Compound Ij-49

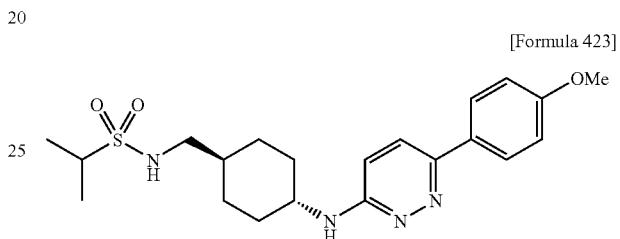
428

[Formula 422]



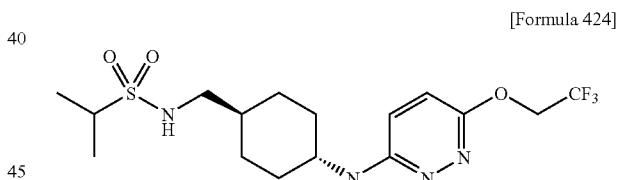
1H-NMR (DMSO-d₆) δ: 0.96-1.28 (m, 4H), 1.22 (d, 6H, J=6.6 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.83 (t, 2H, J=6.0 Hz), 3.10-3.22 (m, 1H), 3.74-3.92 (m, 1H), 3.82 (s, 3H), 6.78-6.88 (m, 2H), 6.92-7.04 (m, 2H), 7.37 (t, 1H, J=7.5 Hz), 7.46-7.58 (m, 2H), 7.79 (d, 1H, J=9.3 Hz)

Compound Ij-50



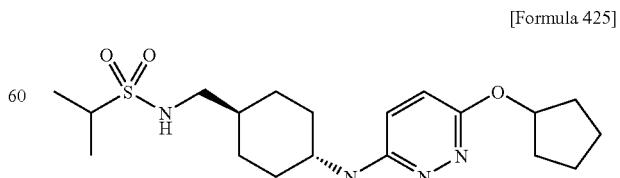
1H-NMR (DMSO-d₆) δ: 0.96-1.28 (m, 4H), 1.22 (d, 6H, J=6.9 Hz), 1.42 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.83 (t, 2H, J=6.0 Hz), 3.10-3.22 (m, 1H), 3.74-3.92 (m, 1H), 3.80 (s, 3H), 6.70 (d, 1H, J=7.8 Hz), 6.82 (d, 1H, J=9.3 Hz), 6.95-7.05 (m, 3H), 7.72 (d, 1H, J=9.3 Hz), 7.90 (d, 2H, J=9.0 Hz).

Compound Ij-51



1H-NMR (DMSO-d₆) δ: 0.92-1.05 (m, 2H), 1.07-1.20 (m, 2H), 1.22 (d, 6H, J=6.9 Hz), 1.39 (m, 1H), 1.76-1.85 (m, 2H), 2.02-2.10 (m, 2H), 2.81 (t, 2H, J=6.3 Hz), 3.09-3.20 (m, 1H), 3.57-3.68 (m, 1H), 4.89-4.98 (m, 2H), 6.47 (d, 1H, J=8.0 Hz), 6.88 (d, 1H, J=7.5 Hz), 6.96 (t, 1H, J=6.0 Hz), 7.02 (d, 1H, J=7.5 Hz).

Compound Ij-52

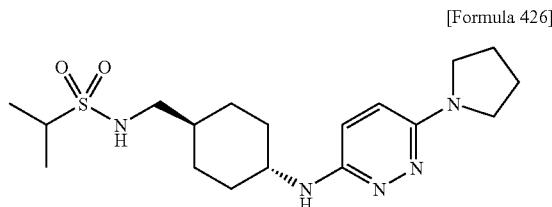


1H-NMR (DMSO-d₆) δ: 0.92-1.05 (m, 2H), 1.07-1.20 (m, 2H), 1.22 (d, 6H, J=6.9 Hz), 1.39 (m, 1H), 1.52-1.74 (m, 6H),

429

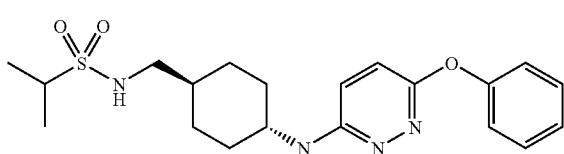
1.77-1.85 (m, 2H), 1.87-1.97 (m, 2H), 2.02-2.09 (m, 2H),
 2.81 (t, 2H, J=6.3 Hz), 3.09-3.20 (m, 1H), 3.55-3.65 (m, 1H),
 5.25-5.32 (m, 1H), 6.19 (d, 1H, J=8.0 Hz), 6.77 (s, 2H), 6.95
 (t, 1H, J=6.0 Hz).

Compound Ij-53



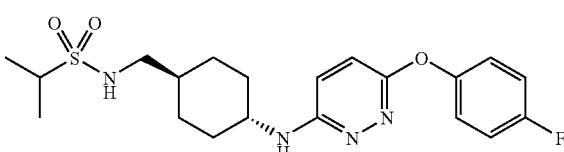
1H-NMR (DMSO-d6) δ: 0.92-1.15 (m, 4H), 1.21 (d, 6H,
 J=6.9 Hz), 1.38 (m, 1H), 1.77-1.85 (m, 2H), 1.88-1.95 (m,
 4H), 2.02-2.09 (m, 2H), 2.80 (t, 2H, J=6.3 Hz), 3.09-3.20 (m,
 1H), 3.25-3.35 (m, 4H), 3.55-3.65 (m, 1H), 5.80-5.85 (m,
 1H), 6.72 (d, 1H, J=8.0 Hz), 6.80 (d, 1H, J=8.0 Hz), 6.96 (t,
 1H, J=6.0 Hz).

Compound Ij-54



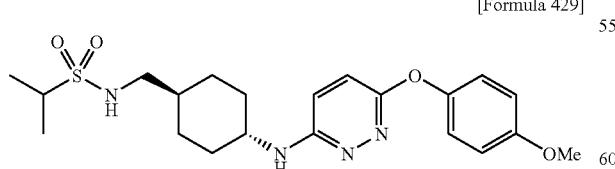
1H-NMR (DMSO-d6) δ: 0.92-1.20 (m, 4H), 1.21 (d, 6H,
 J=6.9 Hz), 1.38 (m, 1H), 1.77-1.85 (m, 2H), 2.02-2.09 (m,
 2H), 2.80 (t, 2H, J=6.3 Hz), 3.09-3.20 (m, 1H), 3.58-3.65 (m,
 1H), 6.56 (d, 1H, J=8.0 Hz), 6.90-6.98 (m, 2H), 7.03-7.10 (m,
 3H), 7.15 (t, 1H, J=8.0 Hz), 6.38 (t, 2H, J=8.0 Hz).

Compound Ij-55



1H-NMR (DMSO-d6) δ: 0.92-1.20 (m, 4H), 1.21 (d, 6H,
 J=6.9 Hz), 1.38 (m, 1H), 1.77-1.85 (m, 2H), 2.02-2.09 (m,
 2H), 2.80 (t, 2H, J=6.3 Hz), 3.09-3.20 (m, 1H), 3.58-3.65 (m,
 1H), 6.55 (d, 1H, J=8.0 Hz), 6.90-6.98 (m, 2H), 7.05-7.15 (m,
 3H), 7.21 (t, 2H, J=8.0 Hz).

Compound Ij-56

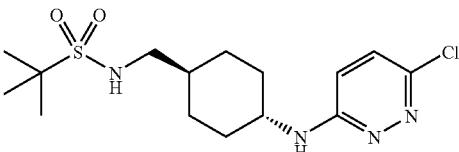


1H-NMR (DMSO-d6) δ: 0.92-1.20 (m, 4H), 1.21 (d, 6H,
 J=6.9 Hz), 1.38 (m, 1H), 1.77-1.85 (m, 2H), 2.02-2.09 (m,
 2H), 2.80 (t, 2H, J=6.3 Hz), 3.09-3.20 (m, 1H), 3.58-3.65 (m,
 1H), 3.75 (s, 3H), 6.49 (d, 1H, J=8.0 Hz), 6.87-6.98 (m, 4H),
 7.00-7.07 (m, 3H).

430

Compound Ij-57

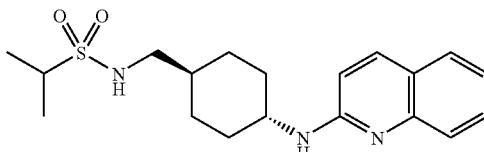
[Formula 430]



1H-NMR (DMSO-d6) δ: 0.96-1.28 (m, 4H), 1.27 (s, 9H),
 1.40 (m, 1H), 1.78-1.88 (m, 2H), 2.00-2.10 (m, 2H), 2.88 (t,
 2H, J=6.0 Hz), 3.60-3.76 (m, 1H), 6.82-6.92 (m, 2H), 6.96 (d,
 1H, J=7.8 Hz), 7.32 (d, 1H, J=9.6 Hz).

Compound Ij-58

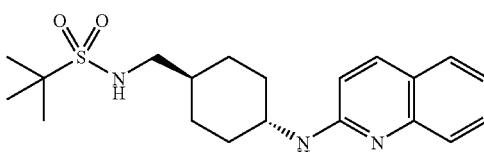
[Formula 431]



1H-NMR (DMSO-d6) δ: 0.99-1.28 (m, 4H), 1.21 (d, 6H,
 J=6.9 Hz), 1.39 (m, 1H), 1.78-1.86 (m, 2H), 2.04-2.10 (m,
 2H), 2.82 (t, 2H, J=6.1 Hz), 3.06-3.20 (m, 1H), 3.80-3.96 (m,
 1H), 6.71 (d, 1H, J=9.0 Hz), 6.76-6.86 (m, 1H), 6.90-6.98 (m,
 1H), 7.10 (t, 1H, J=8.1 Hz), 7.39-7.50 (m, 2H), 7.56 (d, 1H,
 J=7.5 Hz), 7.78 (d, 1H, J=7.5 Hz).

Compound Ij-59

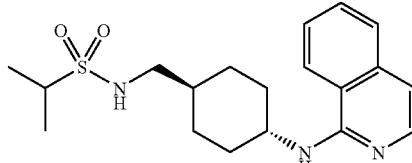
[Formula 432]



1H-NMR (DMSO-d6) δ: 0.99-1.28 (m, 4H), 1.27 (s, 9H),
 1.40 (m, 1H), 1.80-1.85 (m, 2H), 2.04-2.09 (m, 2H), 2.91 (t,
 2H, J=6.1 Hz), 3.80-3.96 (m, 1H), 6.70 (d, 1H, J=9.0 Hz),
 6.81-6.87 (m, 2H), 7.10 (t, 1H, J=8.1 Hz), 7.39-7.44 (m, 2H),
 7.56 (d, 1H, J=7.5 Hz), 7.79 (d, 1H, J=7.5 Hz).

Compound Ij-60

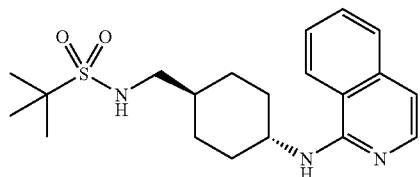
[Formula 433]



1H-NMR (DMSO-d6) δ: 0.97-1.09 (m, 2H), 1.23 (d, 6H,
 J=6.9 Hz), 1.31-1.50 (m, 2H), 1.82-1.87 (m, 2H), 2.01-2.05
 (m, 2H), 2.83 (t, 2H, J=6.0 Hz), 3.11-3.20 (m, 1H), 4.00-4.18
 (m, 1H), 6.83 (d, 1H, J=5.7 Hz), 6.90-7.06 (m, 2H), 7.45 (t,
 1H, J=6.9 Hz), 7.59 (t, 1H, J=8.1 Hz), 7.67 (d, 1H, J=8.4 Hz),
 7.83 (d, 1H, J=5.7 Hz), 8.27 (d, 1H, J=7.5 Hz).

431

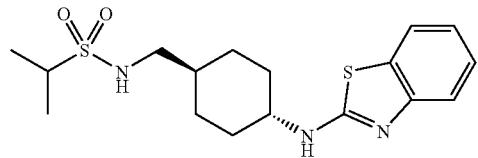
Compound Ij-61



[Formula 434]

1H-NMR (DMSO-d₆) δ: 0.96-1.09 (m, 2H), 1.28 (s, 9H), 1.29-1.50 (m, 2H), 1.82-1.87 (m, 2H), 2.01-2.05 (m, 2H), 2.91 (t, 2H, J=7.8 Hz), 4.00-4.18 (m, 1H), 6.82-6.89 (m, 2H), 6.97 (d, 1H, J=7.5 Hz), 7.45 (t, 1H, J=7.2 Hz), 7.59 (t, 1H, J=8.1 Hz), 7.67 (d, 1H, J=7.8 Hz), 7.84 (d, 1H, J=6.0 Hz), 8.27 (d, 1H, J=8.4 Hz).

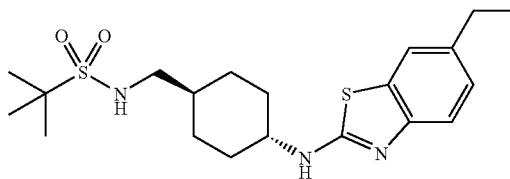
Compound Ij-62



[Formula 435]

1H-NMR (DMSO-d₆) δ: 0.96-1.14 (m, 2H), 1.18-1.30 (m, 2H), 1.22 (d, 6H, J=6.6 Hz), 1.40 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.14 (m, 2H), 2.81 (t, 2H, J=6.3 Hz), 3.10-3.20 (m, 1H), 3.58-3.70 (m, 1H), 6.95-7.03 (m, 2H), 7.20 (t, 1H, J=7.5 Hz), 7.37 (d, 1H, J=8.1 Hz), 7.64 (d, 1H, J=7.5 Hz), 7.92 (d, 1H, J=7.8 Hz).

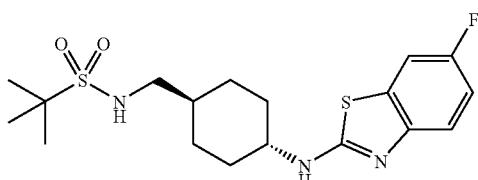
Compound Ij-63



[Formula 436]

1H-NMR (DMSO-d₆) δ: 1.00 (dd, 2H, J=24.8, 10.6 Hz), 1.15-1.22 (m, 2H), 1.18 (t, 3H, J=7.6 Hz), 1.27 (s, 9H), 1.34-1.40 (m, 1H), 1.81 (d, 2H, J=11.6 Hz), 2.07 (d, 2H, J=11.6 Hz), 2.60 (q, 2H, J=7.6 Hz), 2.89 (t, 2H, J=6.3 Hz), 3.52-3.63 (m, 1H), 6.87 (t, 1H, J=5.8 Hz), 7.04 (d, 1H, J=7.9 Hz), 7.27 (d, 1H, J=8.2 Hz), 7.47 (s, 1H), 7.80 (d, 1H, J=7.6 Hz).

Compound Ij-64

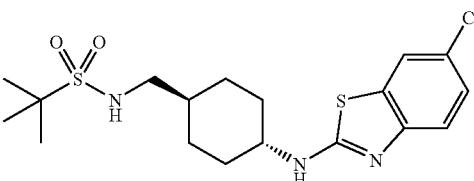


[Formula 437]

1H-NMR (DMSO-d₆) δ: 0.92-1.10 (m, 2H), 1.12-1.25 (m, 2H), 1.27 (s, 9H), 1.37 (m, 1H), 1.76-1.84 (m, 2H), 2.02-2.12 (m, 2H), 2.89 (t, 2H, J=6.0 Hz), 3.50-3.66 (m, 1H), 6.87 (t, 1H, J=5.7 Hz), 7.03 (dd, 1H, J=8.7, 2.7 Hz), 7.32-7.37 (m, 1H), 7.58 (dd, 1H, J=8.7, 2.7 Hz), 7.92 (d, 1H, J=7.2 Hz).

432

Compound Ij-65

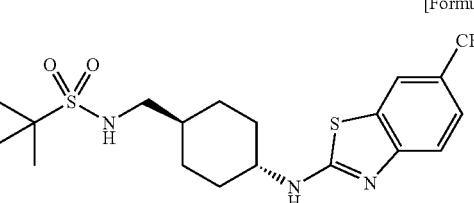


[Formula 438]

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10

1H-NMR (DMSO-d₆) δ: 1.01 (dd, 2H, J=24.6, 10.2 Hz), 1.21 (dd, 2H, J=24.6, 10.2 Hz), 1.27 (s, 9H), 1.34-1.40 (m, 1H), 1.82 (d, 2H, J=11.2 Hz), 2.08 (d, 2H, J=11.2 Hz), 2.89 (t, 2H, J=6.2 Hz), 3.59-3.65 (m, 1H), 6.87 (t, 1H, J=5.8 Hz), 7.21 (dd, 1H, J=8.6, 2.4 Hz), 7.34 (d, 1H, J=8.6 Hz), 7.77 (d, 1H, J=1.8 Hz), 8.06 (d, 1H, J=7.6 Hz).

Compound Ij-66

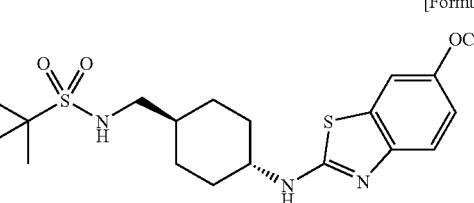


[Formula 439]

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1H-NMR (CDCl₃) δ: 1.09-1.46 (m, 4H), 1.41 (s, 9H), 1.54 (m, 1H), 1.90-2.00 (m, 2H), 2.24-2.34 (m, 2H), 3.09 (t, 2H, J=6.6 Hz), 3.46-3.60 (m, 1H), 3.99 (t, 1H, J=6.6 Hz), 6.58 (brs, 1H), 7.58 (s, 2H), 7.85 (s, 1H).

Compound Ij-67

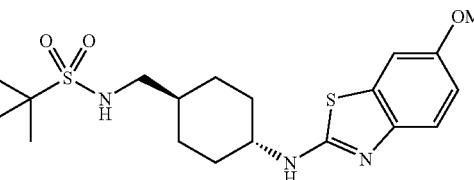


[Formula 440]

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1H-NMR (DMSO-d₆) δ: 0.90-1.30 (m, 4H), 1.27 (s, 9H), 1.30-1.48 (m, 1H), 1.82 (d, 2H, J=11.1 Hz), 2.08 (d, 2H, J=9.6 Hz), 2.89 (t, 2H, J=6.3 Hz), 3.55-3.70 (m, 1H), 6.87 (t, 1H, J=5.7 Hz), 7.17 (m, 1H), 7.41 (d, 1H, J=8.7 Hz), 7.77 (d, 1H, J=1.5 Hz), 8.10 (d, 1H, J=7.5 Hz). ESI(positive) m/z 466.2 [M+H]⁺

Compound Ij-68



[Formula 441]

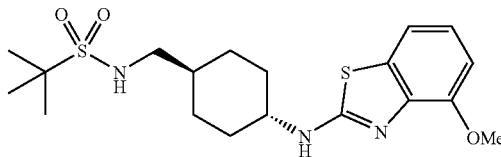
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1H-NMR (DMSO-d₆) δ: 0.90-1.28 (m, 4H), 1.25 (s, 9H), 1.32 (m, 1H), 1.76-1.82 (m, 2H), 2.00-2.10 (m, 2H), 2.87 (t, 2H, J=6.6 Hz), 3.50-3.62 (m, 1H), 3.71 (s, 3H), 6.77 (dd, 1H, J=8.7, 2.7 Hz), 6.84 (t, 1H, J=5.7 Hz), 7.22-7.28 (m, 2H), 7.66 (d, 1H, J=7.2 Hz).

433

Compound Ij-69

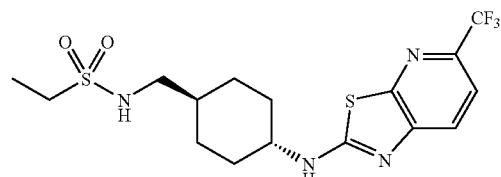
[Formula 442]



¹H-NMR (DMSO-d₆) δ: 0.94-1.10 (m, 2H), 1.12-1.25 (m, 2H), 1.27 (s, 9H), 1.37 (m, 1H), 1.76-1.84 (m, 2H), 2.02-2.12 (m, 2H), 2.90 (t, 2H, J=6.0 Hz), 3.52-3.68 (m, 1H), 3.84 (s, 3H), 6.82 (d, 1H, J=8.1 Hz), 6.88 (t, 1H, J=5.4 Hz), 6.95 (t, 0.1H, J=7.8 Hz), 7.23 (d, 1H, J=7.8 Hz), 7.83 (d, 1H, J=7.8 Hz).

Compound Ij-70

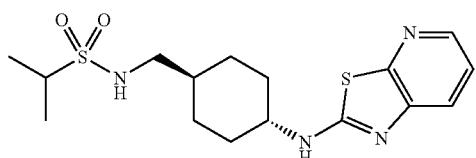
[Formula 443]



¹H-NMR (DMSO-d₆) δ: 0.98-1.10 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.17-1.32 (m, 2H), 1.40 (m, 1H), 1.76-1.88 (m, 2H), 2.04-2.14 (m, 2H), 2.79 (t, 2H, J=6.0 Hz), 2.98 (q, 2H, J=7.2 Hz), 3.60-3.78 (m, 1H), 7.03 (t, 1H, J=6.3 Hz), 7.45-7.54 (m, 2H), 8.10 (s, 1H), 8.34 (d, 1H, J=7.2 Hz).

Compound Ij-71

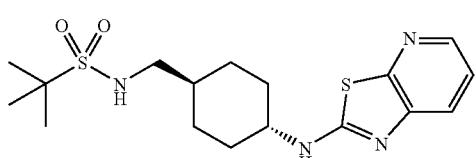
[Formula 444]



¹H-NMR (DMSO-d₆) δ: 1.01 (dd, 2H, J=26.1, 12.3 Hz), 1.16-1.22 (m, 2H), 1.22 (d, 6H, J=6.6 Hz), 1.35-1.41 (m, 1H), 1.70-1.77 (m, 1H), 1.82 (d, 2H, J=11.6 Hz), 2.08 (d, 2H, J=11.6 Hz), 2.81 (t, 2H, J=6.3 Hz), 3.66-3.72 (m, 1H), 6.99 (t, 1H, J=6.3 Hz), 7.23 (dd, 1H, J=8.1, 4.7 Hz), 7.66 (d, 1H, J=8.1 Hz), 8.07 (d, 1H, J=4.7 Hz), 8.26 (d, 1H, J=6.3 Hz).

Compound Ij-72

[Formula 445]



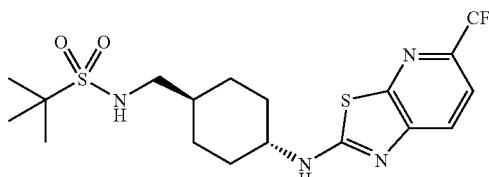
¹H-NMR (DMSO-d₆) δ: 1.01 (dd, 2H, J=24.8, 11.3 Hz), 1.18-1.23 (m, 2H), 1.27 (s, 9H), 1.36-1.39 (m, 1H), 1.82 (d,

434

2H, J=11.5 Hz), 2.08 (d, 2H, J=11.5 Hz), 2.89 (t, 2H, J=6.1 Hz), 3.65-3.73 (m, 1H), 6.87 (t, 1H, J=5.7 Hz), 7.23 (dd, 1H, J=8.1, 4.8 Hz), 7.66 (d, 1H, J=7.9 Hz), 8.07 (d, 1H, J=4.7 Hz), 8.26 (d, 1H, J=7.6 Hz).

5 Compound Ij-73

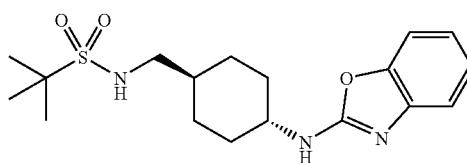
[Formula 446]



¹H-NMR (CDCl₃) δ: 1.09-1.46 (m, 4H), 1.41 (s, 9H), 1.55 (m, 1H), 1.92-2.02 (m, 2H), 2.24-2.34 (m, 2H), 3.09 (t, 2H, J=6.3 Hz), 3.58-3.72 (m, 1H), 3.98 (t, 1H, J=6.0 Hz), 6.30 (brs, 1H), 7.62 (d, 1H, J=8.1 Hz), 7.77 (d, 1H, J=8.4 Hz).

Compound Ij-74

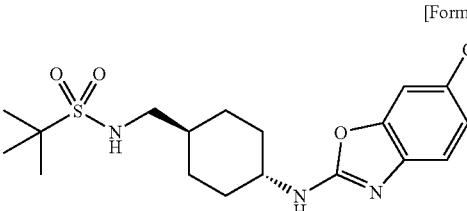
[Formula 447]



¹H-NMR (DMSO-d₆) δ: 0.90-1.08 (m, 2H), 1.12-1.40 (m, 3H), 1.25 (s, 9H), 1.76-1.86 (m, 2H), 1.98-2.10 (m, 2H), 2.87 (d, 2H, J=6.3 Hz), 3.40-3.56 (m, 1H), 6.85 (brs, 1H), 6.93 (t, 1H, J=7.5 Hz), 7.07 (t, 1H, J=7.5 Hz), 7.20 (d, 1H, J=7.5 Hz), 7.29 (d, 1H, J=7.8 Hz), 7.79 (brs, 1H).

Compound Ij-75

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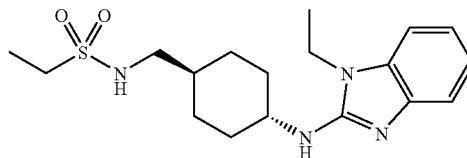


¹H-NMR (CDCl₃) δ: 1.08-1.26 (m, 2H), 1.36-1.60 (m, 3H), 1.40 (s, 9H), 1.92-2.02 (m, 2H), 2.22-2.32 (m, 2H), 3.08 (t, 2H, J=6.6 Hz), 3.68-3.80 (m, 1H), 4.03 (t, 1H, J=6.0 Hz), 7.06 (brs, 1H), 7.20-7.36 (m, 3H).

Compound Ij-76

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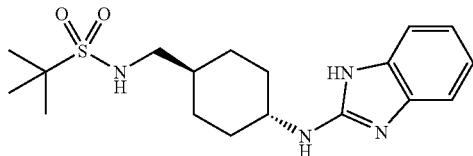
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[Formula 449]

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1H-NMR (DMSO-d₆) δ: 1.02 (dd, 2H, J=25.2, 12.4 Hz), 1.17 (t, 3H, J=7.1 Hz), 1.20 (t, 3H, J=7.3 Hz), 1.26-1.35 (m, 2H), 1.37-1.42 (m, 1H), 1.83 (d, 2H, J=11.6 Hz), 2.05 (d, 2H, J=11.6 Hz), 2.80 (t, 2H, J=6.4 Hz), 2.99 (q, 2H, J=7.3 Hz), 3.65-3.72 (m, 1H), 4.01 (q, 2H, J=7.1 Hz), 6.32 (d, 1H, J=7.9 Hz), 6.86-6.94 (m, 2H), 7.01 (t, 1H, J=6.0 Hz), 7.12 (d, 1H, J=6.9 Hz), 7.17 (d, 1H, J=6.8 Hz).

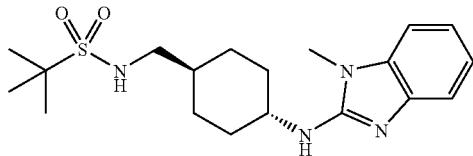
Compound Ij-77



[Formula 450]

1H-NMR (DMSO-d₆) δ: 1.02 (dd, 2H, J=24.8, 10.8 Hz), 1.19-1.21 (m, 2H), 1.30 (s, 9H), 1.37-1.41 (m, 1H), 1.84 (d, 2H, J=10.6 Hz), 2.06 (d, 2H, J=10.6 Hz), 2.92 (t, 2H, J=6.3 Hz), 3.50-3.52 (m, 1H), 6.42 (d, 1H, J=8.1 Hz), 6.83 (d, 1H, J=7.9 Hz), 6.88-6.92 (m, 2H), 7.11-7.14 (m, 2H), 10.58 (s, 1H).

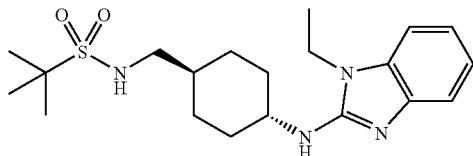
Compound Ij-78



[Formula 451]

1H-NMR (DMSO-d₆) δ: 0.97-1.05 (m, 2H), 1.20-1.26 (m, 2H), 1.28 (s, 9H), 1.34-1.38 (m, 1H), 1.84 (d, 2H, J=11.5 Hz), 2.07 (d, 2H, J=11.5 Hz), 2.90 (t, 2H, J=6.1 Hz), 3.47 (s, 3H), 3.63-3.69 (m, 1H), 6.34 (d, 1H, J=7.6 Hz), 6.87-6.93 (m, 3H), 7.11 (d, 1H, J=8.4 Hz), 7.17 (d, 1H, J=8.4 Hz).

Compound Ij-79



[Formula 452]

1H-NMR (DMSO-d₆) δ: 1.03 (dd, 2H, J=23.6, 10.8 Hz), 1.18 (t, 3H, J=7.5 Hz), 1.25-1.34 (m, 2H), 1.29 (s, 9H), 1.37-1.40 (m, 1H), 1.86 (d, 2H, J=11.7 Hz), 2.07 (d, 2H, J=11.7 Hz), 2.92 (t, 2H, J=6.2 Hz), 3.67-3.73 (m, 1H), 4.03 (q,

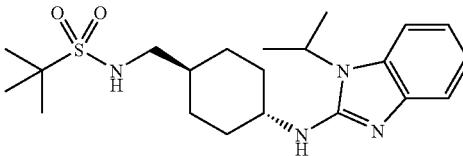
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2H, J=7.1 Hz), 6.34 (d, 1H, J=7.9 Hz), 6.87-6.96 (m, 3H), 7.14 (dd, 1H, J=8.1, 1.2 Hz), 7.19 (dd, 1H, J=8.1, 1.2 Hz).

Compound Ij-80

[Formula 453]



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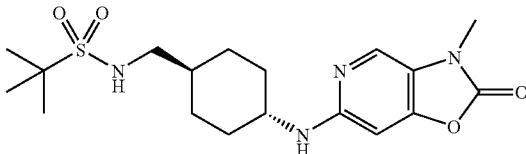
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1H-NMR (DMSO-d₆) δ: 1.00 (dd, 2H, J=23.2, 11.9 Hz), 1.19-1.25 (m, 2H), 1.28 (s, 9H), 1.33-1.38 (m, 1H), 1.45 (s, 3H), 1.47 (s, 3H), 1.83 (d, 2H, J=11.1 Hz), 2.07 (d, 2H, J=11.1 Hz), 2.90 (t, 2H, J=6.1 Hz), 3.62-3.70 (m, 1H), 4.57-4.66 (m, 1H), 6.21 (d, 1H, J=7.9 Hz), 6.82-6.94 (m, 3H), 7.18 (d, 1H, J=7.6 Hz), 7.31 (d, 1H, J=7.6 Hz).

Compound Ij-81

[Formula 454]



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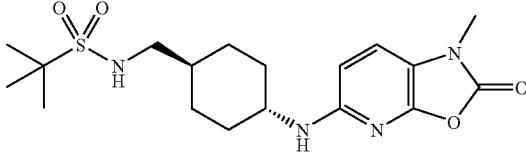
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Compound Ij-82

[Formula 455]



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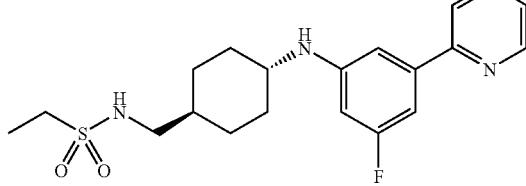
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1H-NMR (DMSO-d₆) δ: 0.90-1.19 (m, 4H), 1.28 (s, 9H), 1.32-1.45 (m, 1H), 1.80 (d, 2H, J=11.2 Hz), 1.98 (d, 2H, J=11.2 Hz), 2.84-2.93 (m, 2H), 3.26 (s, 3H), 3.40-3.53 (m, 1H), 6.29 (d, 1H, J=8.0 Hz), 6.38 (d, 1H, J=7.2 Hz), 6.86 (s, 1H), 7.33 (d, 1H, J=8.4 Hz).

Compound Ij-83

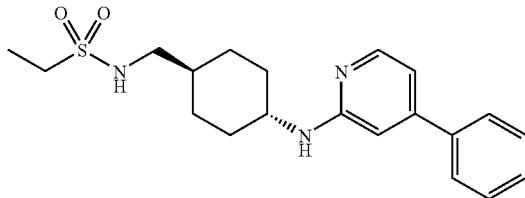
[Formula 456]



437

Compound Ij-84

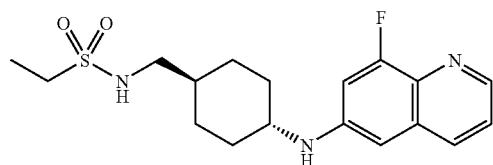
[Formula 457]



1H-NMR (DMSO-d₆) δ: 0.92-1.20 (m, 4H), 1.18 (t, 3H, J=7.2 Hz), 1.40 (m, 1H), 1.75-1.85 (m, 2H), 1.96-2.06 (m, 2H), 2.78 (t, 2H, J=6.0 Hz), 2.98 (q, 2H, J=7.2 Hz), 3.60-3.78 (m, 1H), 6.38 (d, 1H, J=8.1 Hz), 6.67 (s, 1H), 6.72 (d, 1H, J=5.4 Hz), 7.00 (t, 1H, J=6.0 Hz), 7.36-7.54 (m, 3H), 7.62 (d, 2H, J=6.9 Hz), 8.00 (d, 1H, J=5.4 Hz)

Compound Ij-85

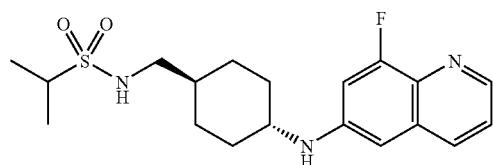
[Formula 458]



1H-NMR (DMSO-d₆) δ: 1.00-1.20 (m, 4H), 1.20 (t, 3H, J=7.2 Hz), 1.43 (m, 1H), 1.80-1.88 (m, 2H), 2.03-2.13 (m, 2H), 2.81 (t, 3H, J=6.0 Hz), 3.00 (q, 2H, J=7.2 Hz), 3.26 (m, 1H), 6.17 (d, 1H, J=7.6 Hz), 6.57 (s, 1H), 6.96-7.07 (m, 2H), 7.35 (dd, 1H, J=8.4, 4.0 Hz), 8.02 (d, 1H, J=8.4 Hz), 8.47 (d, 1H, J=4.0 Hz).

Compound Ij-86

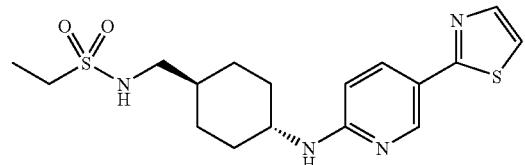
[Formula 459]



1H-NMR (DMSO-d₆) δ: 1.00-1.24 (m, 4H), 1.23 (d, 6H, J=6.4 Hz), 1.42 (m, 1H), 1.80-1.88 (m, 2H), 2.03-2.12 (m, 2H), 2.79-2.87 (m, 2H), 3.16 (m, 1H), 3.27 (m, 1H), 6.17 (d, 1H, J=8.0 Hz), 6.57 (s, 1H), 6.99 (d, 1H, J=8.0 Hz), 7.01 (s, 1H), 7.35 (dd, 1H, J=8.0, 4.0 Hz), 8.02 (d, 1H, J=8.0 Hz), 8.47 (d, 1H, J=2.8 Hz).

Compound Ij-87

[Formula 460]

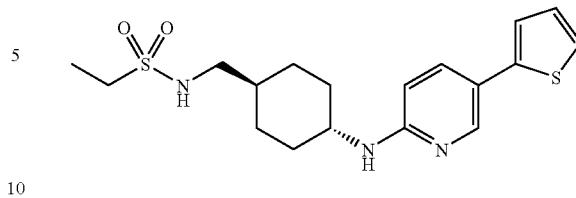


1H-NMR (DMSO-d₆) δ: 0.95-1.08 (m, 2H), 1.11-1.25 (m, 2H), 1.20 (t, 3H, J=7.2 Hz), 1.40 (m, 1H), 1.76-1.86 (m, 2H), 1.97-2.04 (m, 2H), 2.73-2.82 (m, 2H), 2.99 (q, 2H, J=7.2 Hz), 3.70 (m, 1H), 6.53 (d, 1H, J=8.8 Hz), 6.53 (d, 1H, J=8.8 Hz), 7.01 (t, 1H, J=6.0 Hz), 7.58 (d, 1H, J=3.2 Hz), 7.79 (d, 1H, J=3.2 Hz), 7.86 (d, 1H, J=8.8 Hz), 8.55 (s, 1H).

438

Compound Ij-88

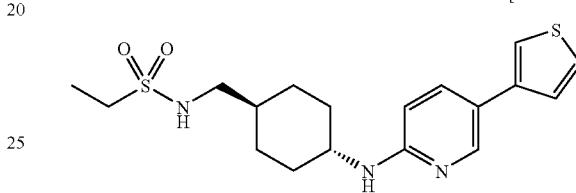
[Formula 461]



1H-NMR (DMSO-d₆) δ: 0.92-1.07 (m, 2H), 1.09-1.20 (m, 2H), 1.19 (t, 6H, J=7.2 Hz), 1.39 (m, 1H), 1.75-1.83 (m, 2H), 1.95-2.03 (m, 2H), 2.74-2.81 (m, 2H), 2.98 (q, 2H, J=7.2 Hz), 3.66 (m, 1H), 6.48 (d, 1H, J=8.4 Hz), 6.60 (d, 1H, J=7.6 Hz), 7.00 (t, 1H, J=5.6 Hz), 7.06 (dd, 1H, J=4.8, 2.4 Hz), 7.25 (d, 1H, J=2.4 Hz), 7.37 (d, 1H, J=4.8 Hz), 7.60 (dd, 1H, J=8.4, 2.0 Hz), 8.26 (s, 1H).

Compound Ij-89

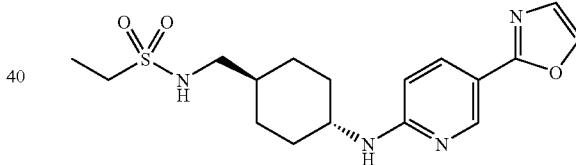
[Formula 462]



1H-NMR (DMSO-d₆) δ: 0.93-1.07 (m, 2H), 1.10-1.20 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.39 (m, 1H), 1.76-1.84 (m, 2H), 1.96-2.04 (m, 2H), 2.73-2.81 (m, 2H), 2.98 (q, 2H, J=7.2 Hz), 3.65 (m, 1H), 6.41-6.50 (m, 2H), 7.01 (t, 1H, J=6.0 Hz), 7.44 (d, 1H, J=4.0 Hz), 7.58 (m, 1H), 7.59 (s, 1H), 7.68 (d, 1H, J=8.0 Hz), 8.34 (s, 1H).

Compound Ij-90

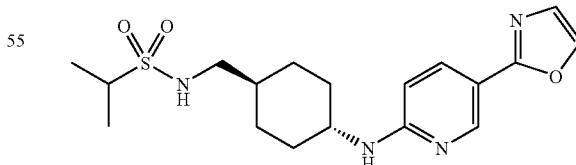
[Formula 463]



1H-NMR (DMSO-d₆) δ: 0.95-1.08 (m, 2H), 1.12-1.25 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.39 (m, 1H), 1.76-1.86 (m, 2H), 1.94-2.03 (m, 2H), 2.75-2.82 (m, 2H), 2.98 (q, 2H, J=7.2 Hz), 3.71 (m, 1H), 6.54 (d, 1H, J=8.8 Hz), 6.98-7.07 (m, 2H), 7.25 (s, 1H), 7.85 (dd, 1H, J=8.8, 2.0 Hz), 8.07 (s, 1H), 8.56 (d, 1H, J=2.0 Hz).

Compound Ij-91

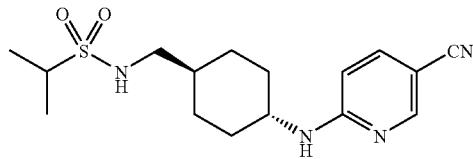
[Formula 464]



1H-NMR (DMSO-d₆) δ: 0.93-1.07 (m, 2H), 1.11-1.22 (m, 2H), 1.21 (d, 6H, J=6.8 Hz), 1.38 (m, 1H), 1.77-1.85 (m, 2H), 1.95-2.03 (m, 2H), 2.77-2.83 (m, 2H), 3.14 (m, 1H), 3.72 (m, 1H), 6.53 (d, 1H, J=8.8 Hz), 6.97 (t, 1H, J=6.0 Hz), 7.02 (d, 1H, J=7.6 Hz), 7.25 (s, 1H), 7.84 (dd, 1H, J=8.8, 2.0 Hz), 8.06 (s, 1H), 8.56 (d, 1H, J=2.0 Hz).

439

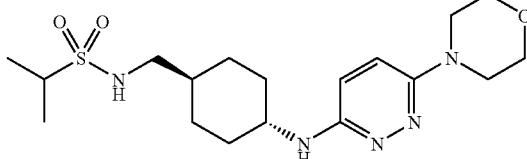
Compound Ij-92



[Formula 465]

1H-NMR (DMSO-d₆) δ: 0.92-1.03 (m, 2H), 1.11-1.23 (m, 2H), 1.21 (d, 6H, J=6.8 Hz), 1.37 (m, 1H), 1.75-1.83 (m, 2H), 1.91-1.99 (m, 2H), 2.36-2.42 (m, 2H), 3.12 (m, 1H), 3.70 (m, 1H), 6.49 (d, 1H, J=9.2 Hz), 6.97 (t, 1H, J=6.0 Hz), 7.47 (d, 1H, J=8.0 Hz), 7.62 (d, 1H, J=8.0 Hz), 8.36 (s, 1H).

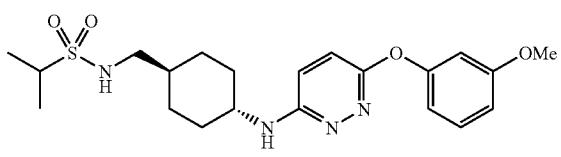
Compound Ij-93



[Formula 466]

1H-NMR (DMSO-d₆) δ: 0.95-1.13 (m, 4H), 1.23 (d, 6H, J=6.9 Hz), 1.31-1.44 (m, 1H), 1.78-1.82 (m, 2H), 2.03-2.06 (m, 2H), 2.76-2.82 (m, 2H), 3.10-3.19 (m, 1H), 3.20-3.25 (m, 4H), 3.58-3.65 (m, 1H), 3.69-3.74 (m, 4H), 6.04 (d, 1H, J=7.5 Hz), 6.72 (d, 1H, J=9.6 Hz), 6.95-6.99 (m, 1H), 7.10 (d, 1H, J=9.6 Hz).

Compound Ij-94

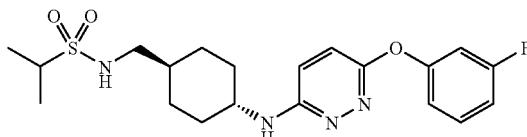


[Formula 467]

1H-NMR (DMSO-d₆) δ: 0.96-1.42 (m, 5H), 1.22 (d, 6H, J=6.9 Hz), 1.79-1.83 (m, 2H), 2.03-2.07 (m, 2H), 2.80 (d, 2H, J=6.3 Hz), 3.10-3.19 (m, 1H), 3.54-3.70 (m, 1H), 3.74 (s, 3H), 6.57-6.64 (m, 3H), 6.72-6.75 (m, 1H), 6.90-7.09 (m, 3H), 7.24-7.30 (m, 1H).

Compound Ij-95

[Formula 468]



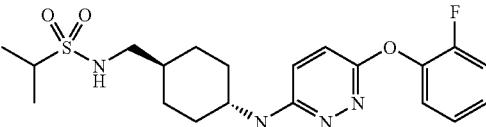
60

1H-NMR (DMSO-d₆) δ: 0.93-1.04 (m, 2H), 1.10-1.18 (m, 2H), 1.21 (d, 6H, J=6.6 Hz), 1.34-1.44 (m, 1H), 1.78-1.87 (m, 2H), 2.02-2.12 (m, 2H), 2.77-2.84 (m, 2H), 3.10-3.20 (m, 1H), 3.52-3.70 (m, 1H), 6.64 (d, 1H, J=8.0 Hz), 6.88-7.06 (m, 5H), 7.12 (d, 1H, J=8.0 Hz), 7.37-7.46 (m, 1H).

440

Compound Ij-96

[Formula 469]

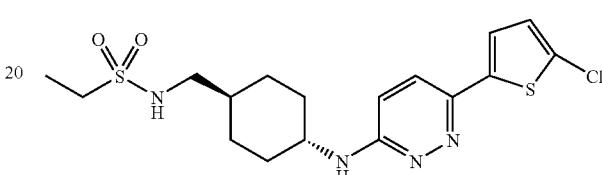


10

1H-NMR (DMSO-d₆) δ: 0.90-1.04 (m, 2H), 1.05-1.18 (m, 2H), 1.21 (d, 6H, J=6.6 Hz), 1.33-1.43 (m, 1H), 1.75-1.84 (m, 2H), 1.98-2.08 (m, 2H), 2.76-2.84 (m, 2H), 3.08-3.18 (m, 1H), 3.52-3.64 (m, 1H), 6.55 (d, 1H, J=8.0 Hz), 6.91-7.00 (m, 2H), 7.15-7.38 (m, 5H).

Compound Ij-97

[Formula 470]

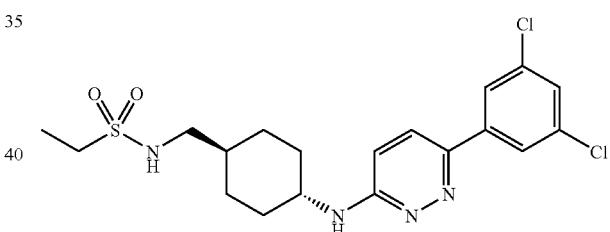


20

1H-NMR (DMSO-d₆) δ: 0.96-1.08 (m, 2H), 1.12-1.25 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.35-1.47 (m, 1H), 1.78-1.87 (m, 2H), 2.02-2.10 (m, 2H), 2.78-2.83 (m, 2H), 2.98 (q, 2H, J=7.2 Hz), 3.70-3.82 (m, 1H), 6.82 (d, 1H, J=8.0 Hz), 6.93 (d, 1H, J=8.0 Hz), 7.01 (t, 1H, J=4.5 Hz), 7.13 (d, 1H, J=4.0 Hz), 7.43 (d, 1H, J=4.0 Hz), 7.76 (d, 1H, J=8.0 Hz).

Compound Ij-98

[Formula 471]

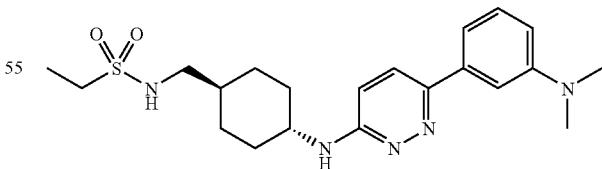


35

1H-NMR (DMSO-d₆) δ: 0.97-1.10 (m, 2H), 1.17-1.28 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.37-1.49 (m, 1H), 1.80-1.88 (m, 2H), 2.04-2.12 (m, 2H), 2.77-2.83 (m, 2H), 2.99 (q, 2H, J=7.2 Hz), 3.76-3.88 (m, 1H), 6.85 (d, 1H, J=8.0 Hz), 6.99-7.05 (m, 2H), 7.61 (s, 1H), 7.90 (d, 1H, J=8.0 Hz), 8.02 (s, 2H).

Compound Ij-99

[Formula 472]



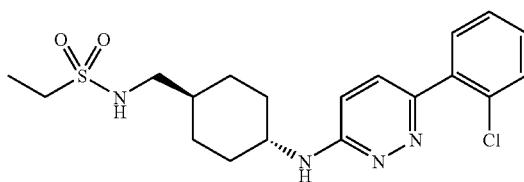
60

1H-NMR (DMSO-d₆) δ: 0.98-1.10 (m, 2H), 1.14-1.26 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.37-1.48 (m, 1H), 1.80-1.88 (m, 2H), 2.04-2.13 (m, 2H), 2.77-2.83 (m, 2H), 2.96 (s, 6H), 2.99 (q, 2H, J=7.2 Hz), 3.76-3.86 (m, 1H), 6.72-6.78 (m, 2H), 6.82 (d, 1H, J=8.0 Hz), 7.02 (t, 1H, J=4.5 Hz), 7.18 (d, 1H, J=8.0 Hz), 7.26 (t, 1H, J=8.0 Hz), 7.34 (s, 1H), 7.74 (d, 1H, J=8.0 Hz).

441

Compound Ij-100

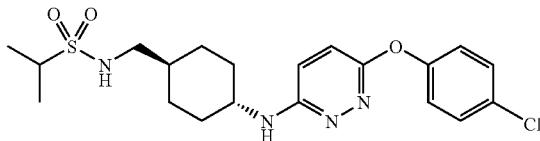
[Formula 473]



1H-NMR (DMSO-d₆) δ: 0.98-1.10 (m, 2H), 1.16-1.27 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.37-1.48 (m, 1H), 1.80-1.88 (m, 2H), 2.04-2.13 (m, 2H), 2.77-2.83 (m, 2H), 2.99 (q, 2H, J=7.2 Hz), 3.76-3.86 (m, 1H), 6.83 (d, 1H, J=8.0 Hz), 6.89 (d, 1H, J=8.0 Hz), 7.02 (t, 1H, J=4.5 Hz), 7.42-7.50 (m, 3H), 7.53-7.59 (m, 2H).

Compound Ij-101

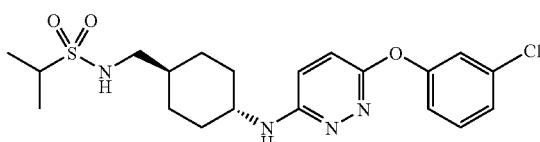
[Formula 474]



1H-NMR (DMSO-d₆) δ: 0.92-1.05 (m, 2H), 1.08-1.20 (m, 2H), 1.21 (d, 6H, J=6.6 Hz), 1.36-1.43 (m, 1H), 1.76-1.84 (m, 2H), 2.02-2.09 (m, 2H), 2.77-2.83 (m, 2H), 3.10-3.20 (m, 1H), 3.56-3.68 (m, 1H), 6.62 (d, 1H, J=8.0 Hz), 6.93 (d, 1H, J=8.0 Hz), 6.98 (t, 1H, J=4.5 Hz), 7.10-7.15 (m, 3H), 7.43 (d, 2H, J=8.0 Hz).

Compound Ij-102

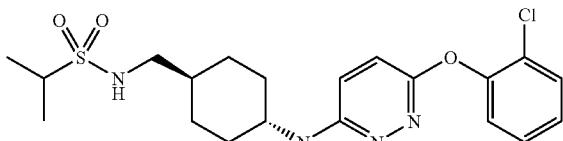
[Formula 475]



1H-NMR (DMSO-d₆) δ: 0.92-1.05 (m, 2H), 1.08-1.20 (m, 2H), 1.21 (d, 6H, J=6.6 Hz), 1.36-1.43 (m, 1H), 1.76-1.84 (m, 2H), 2.02-2.09 (m, 2H), 2.77-2.83 (m, 2H), 3.10-3.20 (m, 1H), 3.57-3.68 (m, 1H), 6.65 (d, 1H, J=8.0 Hz), 6.94 (d, 1H, J=8.0 Hz), 6.97 (t, 1H, J=4.5 Hz), 7.06 (d, 1H, J=8.0 Hz), 7.13 (d, 1H, J=8.0 Hz), 7.18-7.26 (m, 2H), 7.41 (t, 1H, J=8.0 Hz).

Compound Ij-103

[Formula 476]



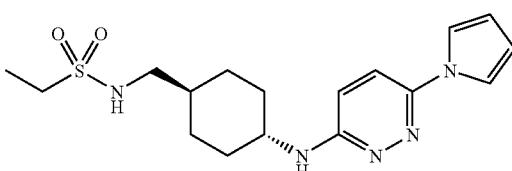
1H-NMR (DMSO-d₆) δ: 0.88-1.04 (m, 2H), 1.05-1.20 (m, 2H), 1.21 (d, 6H, J=6.6 Hz), 1.33-1.43 (m, 1H), 1.77-1.82 (m,

442

2H), 2.00-2.07 (m, 2H), 2.76-2.82 (m, 2H), 3.08-3.20 (m, 1H), 3.52-3.64 (m, 1H), 6.57 (d, 1H, J=8.0 Hz), 6.92-7.00 (m, 2H), 7.17 (d, 1H, J=8.0 Hz), 7.23-7.28 (m, 2H), 7.38 (t, 1H, J=8.0 Hz), 7.56 (d, 1H, J=8.0 Hz).

5 Compound Ij-104

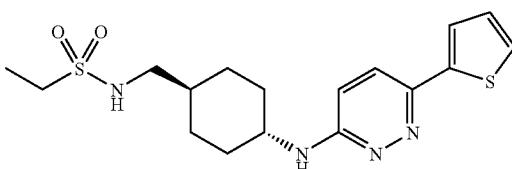
[Formula 477]



1H-NMR (DMSO-d₆) δ: 0.96-1.08 (m, 2H), 1.12-1.24 (m, 2H), 1.19 (t, 3H, J=7.6 Hz), 1.35-1.46 (m, 1H), 1.78-1.86 (m, 2H), 2.04-2.12 (m, 2H), 2.76-2.82 (m, 2H), 2.98 (q, 2H, J=7.6 Hz), 3.67-3.78 (m, 1H), 6.27 (s, 2H), 6.71 (d, 1H, J=8.0 Hz), 6.93 (d, 1H, J=8.0 Hz), 7.02 (brs, 1H), 7.52 (s, 2H), 7.67 (d, 1H, J=8.0 Hz).

Compound Ij-105

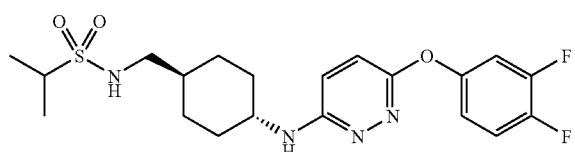
[Formula 478]



1H-NMR (DMSO-d₆) δ: 0.96-1.08 (m, 2H), 1.13-1.25 (m, 2H), 1.19 (t, 3H, J=7.6 Hz), 1.35-1.46 (m, 1H), 1.78-1.87 (m, 2H), 2.04-2.12 (m, 2H), 2.76-2.83 (m, 2H), 2.99 (q, 2H, J=7.6 Hz), 3.72-3.82 (m, 1H), 6.82 (d, 1H, J=8.0 Hz), 6.85 (d, 1H, J=8.0 Hz), 7.03 (t, 1H, J=4.5 Hz), 7.12 (t, 1H, J=4.0 Hz), 7.51 (d, 1H, J=4.0 Hz), 7.56 (d, 1H, J=4.0 Hz), 7.76 (d, 1H, J=8.0 Hz).

Compound Ij-106

[Formula 479]

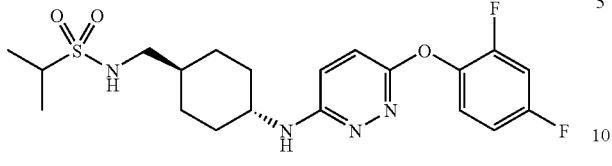


1H-NMR (DMSO-d₆) δ: 0.88-1.02 (m, 2H), 1.07-1.20 (m, 2H), 1.21 (d, 6H, J=6.6 Hz), 1.33-1.45 (m, 1H), 1.76-1.85 (m, 2H), 2.02-2.08 (m, 2H), 2.76-2.83 (m, 2H), 3.10-3.20 (m, 1H), 3.57-3.67 (m, 1H), 6.63 (d, 1H, J=8.0 Hz), 6.92-7.00 (m, 3H), 7.13 (d, 1H, J=8.0 Hz), 7.29-7.36 (m, 1H), 7.42-7.50 (m, 1H).

443

Compound Ij-107

[Formula 480]



¹H-NMR (DMSO-d₆) δ: 0.88-1.02 (m, 2H), 1.07-1.20 (m, 2H), 1.21 (d, 6H, J=6.6 Hz), 1.33-1.43 (m, 1H), 1.75-1.83 (m, 2H), 1.98-2.06 (m, 2H), 2.76-2.83 (m, 2H), 3.08-3.18 (m, 1H), 3.52-3.63 (m, 1H), 6.57 (d, 1H, J=8.0 Hz), 6.93 (d, 1H, J=8.0 Hz), 6.97 (t, 1H, J=4.5 Hz), 7.12 (t, 1H, J=4.0 Hz), 7.19 (d, 1H, J=8.0 Hz), 7.33-7.47 (m, 2H).

Compound Ij-108

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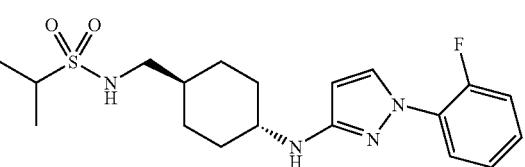
Compound Ij-111

[Formula 484]

1H, J=7.6 Hz), 5.80 (s, 1H), 6.83 (d, 1H, J=6.0 Hz), 7.15-7.40 (m, 3H), 7.75 (t, 1H, J=8.4 Hz), 7.86 (s, 1H).

Compound Ij-111

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¹H-NMR (DMSO-d₆) δ: 0.88-1.02 (m, 2H), 1.07-1.20 (m, 2H), 1.21 (d, 6H, J=6.6 Hz), 1.33-1.43 (m, 1H), 1.75-1.83 (m, 2H), 1.98-2.06 (m, 2H), 2.76-2.83 (m, 2H), 3.08-3.18 (m, 1H), 3.52-3.63 (m, 1H), 6.57 (d, 1H, J=8.0 Hz), 6.93 (d, 1H, J=8.0 Hz), 6.97 (t, 1H, J=4.5 Hz), 7.12 (t, 1H, J=4.0 Hz), 7.19 (d, 1H, J=8.0 Hz), 7.33-7.47 (m, 2H).

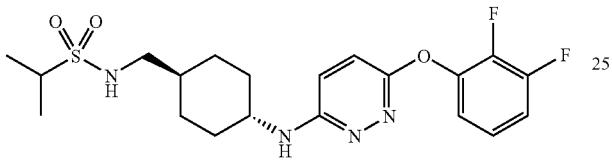
Compound Ij-108

15

¹H-NMR (DMSO-d₆) δ: 0.91-1.19 (m, 4H), 1.21 (d, 6H, J=6.9 Hz), 1.32-1.43 (m, 1H), 1.76-1.82 (m, 2H), 2.02-2.12 (m, 2H), 2.77-2.83 (m, 2H), 3.08-3.27 (m, 2H), 5.48 (d, 1H, J=8.1 Hz), 5.80 (d, 1H, J=2.7 Hz), 6.95 (t, 1H, J=6.0 Hz), 7.15-7.39 (m, 3H), 7.75 (td, 1H, J=8.4, 1.8 Hz), 7.86 (t, 1H, J=2.7 Hz).

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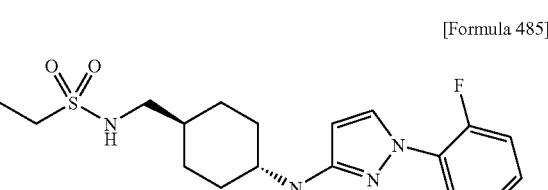
Compound Ij-112



¹H-NMR (DMSO-d₆) δ: 0.88-1.02 (m, 2H), 1.07-1.20 (m, 2H), 1.21 (d, 6H, J=6.6 Hz), 1.33-1.43 (m, 1H), 1.75-1.83 (m, 2H), 1.98-2.07 (m, 2H), 2.76-2.83 (m, 2H), 3.08-3.18 (m, 1H), 3.54-3.63 (m, 1H), 6.63 (d, 1H, J=8.0 Hz), 6.93-7.00 (m, 2H), 7.14 (t, 1H, J=8.0 Hz), 7.20-7.37 (m, 3H).

Compound Ij-109

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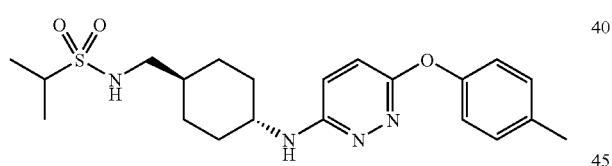


35

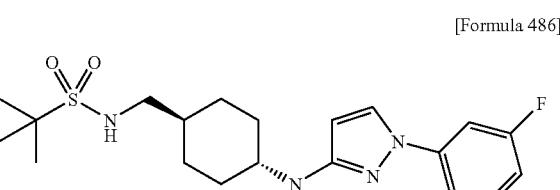
¹H-NMR (DMSO-d₆) δ: 0.91-1.19 (m, 4H), 1.18 (t, 3H, J=7.2 Hz), 1.30-1.45 (m, 1H), 1.76-1.82 (m, 2H), 2.02-2.12 (m, 2H), 2.77-2.83 (m, 2H), 2.98 (q, 2H, J=7.2 Hz), 3.10-3.30 (m, 1H), 5.48 (d, 1H, J=7.8 Hz), 5.80 (d, 1H, J=2.7 Hz), 6.99 (t, 1H, J=6.0 Hz), 7.15-7.40 (m, 3H), 7.75 (td, 1H, J=8.4, 1.8 Hz), 7.86 (t, 1H, J=2.7 Hz).

Compound Ij-113

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¹H-NMR (DMSO-d₆) δ: 0.82-1.05 (m, 2H), 1.05-1.20 (m, 2H), 1.21 (d, 6H, J=6.6 Hz), 1.32-1.43 (m, 1H), 1.76-1.83 (m, 2H), 2.00-2.08 (m, 2H), 2.29 (s, 3H), 2.76-2.83 (m, 2H), 3.08-3.18 (m, 1H), 3.56-3.66 (m, 1H), 6.55 (d, 1H, J=8.0 Hz), 6.90 (d, 1H, J=8.0 Hz), 6.93-7.00 (m, 3H), 7.05 (d, 1H, J=8.0 Hz), 7.17 (d, 2H, J=8.0 Hz).

Compound Ij-110

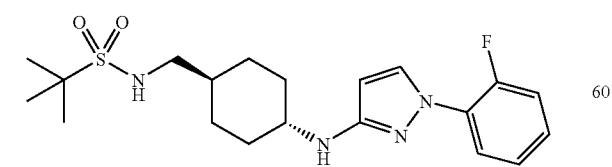
50



55

Compound Ij-114

60



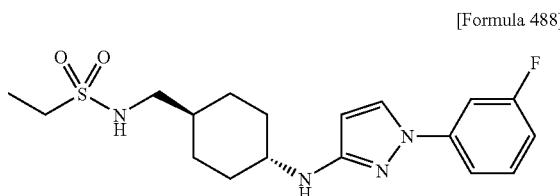
¹H-NMR (DMSO-d₆) δ: 0.91-1.19 (m, 4H), 1.28 (s, 9H), 1.32-1.43 (m, 1H), 1.80 (d, 2H, J=12.0 Hz), 2.07 (d, 2H, J=12.0 Hz), 2.88 (t, 2H, J=6.4 Hz), 3.16-3.27 (m, 1H), 5.47 (d,

[Formula 486]

[Formula 487]

445

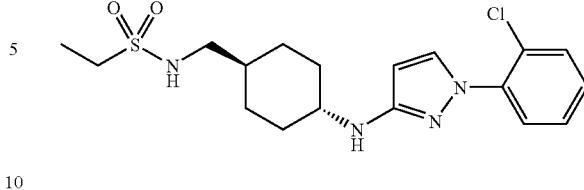
Compound Ii-115



[Formula 488]

1H-NMR (DMSO-d₆) δ: 0.92-1.19 (m, 4H), 1.19 (t, 3H, J=7.2 Hz), 1.30-1.45 (m, 1H), 1.76-1.84 (m, 2H), 2.02-2.12 (m, 2H), 2.74-2.82 (m, 2H), 2.98 (q, 2H, J=7.2 Hz) 3.15-3.30 (m, 1H), 5.53 (d, 1H, J=8.1 Hz), 5.80 (d, 1H, J=2.4 Hz), 6.92 (t, 1H, J=8.4 Hz), 7.01 (t, 1H, J=6.0 Hz), 7.37-7.43 (m, 3H), 8.21 (d, 1H, J=2.4 Hz).

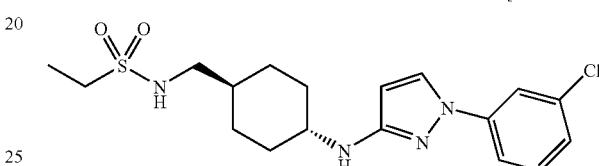
Compound Ij-116



1H-NMR (DMSO-d₆) δ: 0.88-1.19 (m, 4H), 1.18 (t, 3H, J=7.5 Hz), 1.28-1.45 (m, 1H), 1.73-1.83 (m, 2H), 2.02-2.13 (m, 2H), 2.73-2.81 (m, 2H), 2.95 (q, 2H, J=7.5 Hz) 3.12-3.30 (m, 1H), 5.36 (d, 1H, J=7.5 Hz), 5.76 (d, 1H, J=2.4 Hz), 6.98 (t, 1H, J=6.0 Hz), 7.30 (td, 1H, J=7.5, 1.8 Hz), 7.42 (td, 1H, J=7.8, 1.5 Hz), 7.53-7.60 (m, 2H), 7.84 (d, 1H, J=2.7 Hz).

Compound Ij-120

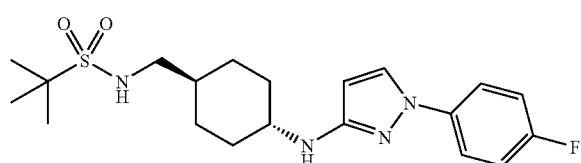
[Formula 492]



1H-NMR (DMSO-d₆) δ: 0.92-1.19 (m, 4H), 1.19 (t, 3H, J=7.5 Hz), 1.30-1.45 (m, 1H), 1.74-1.84 (m, 2H), 2.02-2.10 (m, 2H), 2.75-2.82 (m, 2H), 2.97 (q, 2H, J=7.5 Hz) 3.20-3.30 (m, 1H), 5.52 (d, 1H, J=7.8 Hz), 5.80 (d, 1H, J=2.4 Hz), 6.99 (t, 1H, J=6.0 Hz), 7.13 (d, 1H, J=8.1 Hz), 7.40 (t, 1H, J=8.1 Hz), 7.62 (d, 1H, J=8.4 Hz), 7.72 (s, 1H), 8.22 (d, 1H, J=2.4 Hz).

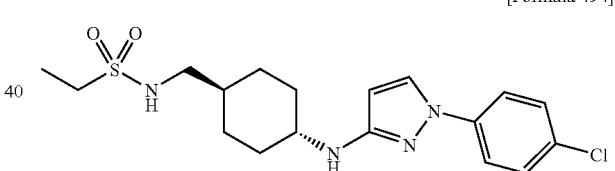
Compound Ij-121

[Formula 493]



[Formula 489]

Compound Ij-117

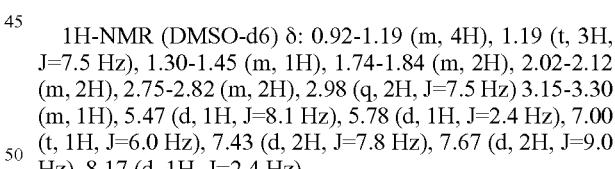


[Formula 494]

1H-NMR (DMSO-d₆) δ: 0.92-1.19 (m, 4H), 1.19 (t, 3H, J=7.5 Hz), 1.30-1.45 (m, 1H), 1.74-1.84 (m, 2H), 2.02-2.12 (m, 2H), 2.75-2.82 (m, 2H), 2.98 (q, 2H, J=7.5 Hz) 3.15-3.30 (m, 1H), 5.47 (d, 1H, J=8.1 Hz), 5.78 (d, 1H, J=2.4 Hz), 7.00 (t, 1H, J=6.0 Hz), 7.43 (d, 2H, J=7.8 Hz), 7.67 (d, 2H, J=9.0 Hz), 8.17 (d, 1H, J=2.4 Hz).

Compound Ij-122

Compound Ij-118

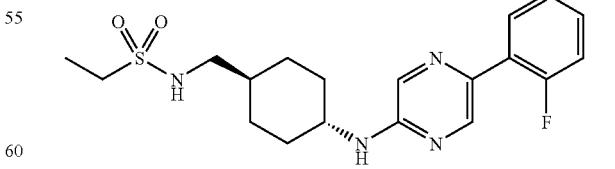
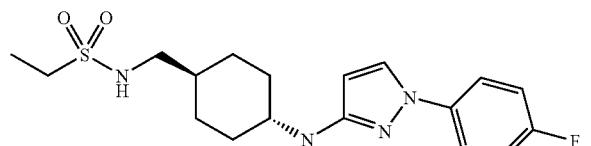


[Formula 490]

1H-NMR (DMSO-d₆) δ: 0.92-1.19 (m, 4H), 1.19 (t, 3H, J=7.5 Hz), 1.30-1.45 (m, 1H), 1.74-1.84 (m, 2H), 2.02-2.12 (m, 2H), 2.75-2.82 (m, 2H), 2.98 (q, 2H, J=7.5 Hz) 3.15-3.30 (m, 1H), 5.47 (d, 1H, J=8.1 Hz), 5.78 (d, 1H, J=2.4 Hz), 7.00 (t, 1H, J=6.0 Hz), 7.43 (d, 2H, J=7.8 Hz), 7.67 (d, 2H, J=9.0 Hz), 8.17 (d, 1H, J=2.4 Hz).

[Formula 491]

Compound Ij-118



[Formula 495]

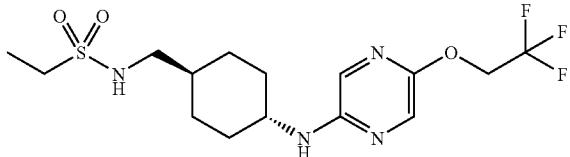
1H-NMR (DMSO-d₆) δ: 0.92-1.19 (m, 4H), 1.19 (t, 3H, J=7.5 Hz), 1.30-1.45 (m, 1H), 1.75-1.86 (m, 2H), 2.02-2.12 (m, 2H), 2.74-2.83 (m, 2H), 2.97 (q, 2H, J=7.5 Hz) 3.13-3.30 (m, 1H), 5.38 (d, 1H, J=8.4 Hz), 5.75 (d, 1H, J=2.7 Hz), 6.99 (t, 1H, J=6.3 Hz), 7.18-7.28 (m, 2H), 7.63-7.70 (m, 2H), 8.11 (d, 1H, J=2.7 Hz).

1H-NMR (DMSO-d₆) δ: 0.94-1.07 (m, 4H), 1.19 (t, 3H, J=7.2 Hz), 1.32-1.50 (m, 1H), 1.81-1.84 (m, 2H), 1.99-2.07 (m, 2H), 2.77-2.81 (m, 2H), 2.98 (q, 2H, J=7.2 Hz) 3.60-3.77 (m, 1H), 7.01-7.05 (m, 1H), 7.22-7.40 (m, 4H), 7.81-7.87 (m, 1H), 8.02 (s, 1H), 8.36 (s, 1H).

447

Compound Ij-123

[Formula 496]

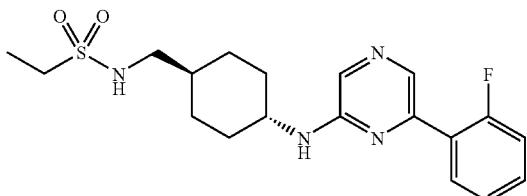


10

1H-NMR (DMSO-d₆) δ: 0.95-1.12 (m, 4H), 1.18 (t, 3H, J=7.2 Hz), 1.32-1.50 (m, 1H), 1.77-1.81 (m, 2H), 1.96-1.99 (m, 2H), 2.74-2.78 (m, 2H), 2.97 (q, 2H, J=7.2 Hz), 3.54-3.70 (m, 1H), 4.81 (q, 2H, J=9.0 Hz), 6.50-6.53 (m, 1H), 6.99-7.03 (m, 1H), 7.50 (d, 1H, J=0.9 Hz) 7.83 (d, 1H, J=0.9 Hz).

Compound Ij-124

[Formula 497]

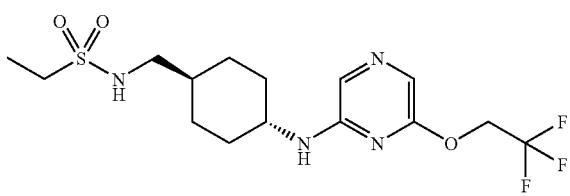


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1H-NMR (DMSO-d₆) δ: 0.95-1.23 (m, 4H), 1.19 (t, 3H, J=7.2 Hz), 1.32-1.50 (m, 1H), 1.77-1.81 (m, 2H), 2.03-2.07 (m, 2H), 2.74-2.80 (m, 2H), 2.97 (q, 2H, J=7.2 Hz), 3.61-3.73 (m, 1H), 7.00-7.04 (m, 1H), 7.09-7.12 (m, 1H), 7.29-7.37 (m, 2H), 7.45-7.52 (m, 1H), 7.88-7.94 (m, 2H), 8.04-8.05 (m, 1H).

Compound Ij-125

[Formula 498]



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1H-NMR (DMSO-d₆) δ: 0.94-1.14 (m, 4H), 1.19 (t, 3H, J=7.2 Hz), 1.32-1.50 (m, 1H), 1.79-1.83 (m, 2H), 1.97-2.03 (m, 2H), 2.76-2.81 (m, 2H), 2.98 (q, 2H, J=7.2 Hz), 3.50-3.63 (m, 1H), 4.43 (q, 2H, J=9.0 Hz), 7.00-7.04 (m, 1H), 7.13-7.15 (m, 1H), 7.35 (s, 1H) 7.55 (s, 1H).

Compound Ij-126

45

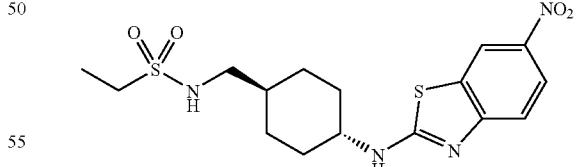
1H-NMR (DMSO-d₆) δ: 0.98-1.07 (m, 2H), 1.15-1.26 (m, 8H), 1.32-1.43 (m, 1H), 1.78-1.84 (m, 2H), 1.98-2.09 (m, 2H), 2.60 (q, 2H, J=7.5 Hz), 2.78 (t, 2H, J=6.3 Hz), 2.96 (q, 2H, J=7.5 Hz), 3.55-3.64 (m, 1H), 6.98-7.05 (m, 2H), 7.27 (dd, 1H, J=7.8, 1.8 Hz), 7.47 (m, 1H), 7.84 (d, 1H, J=7.5 Hz).

Compound Ij-129

50

1H-NMR (DMSO-d₆) δ: 0.92-1.15 (m, 2H), 1.15-1.35 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.33-1.48 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.78-2.84 (m, 2H), 2.97 (q, 2H, J=7.2 Hz), 3.62-3.80 (m, 1H), 7.02 (t, 1H, J=6.0 Hz), 7.45 (d, 1H, J=9.0 Hz), 8.09 (dd, 1H, J=9.0, 2.4 Hz), 8.68 (d, 1H, J=2.4 Hz), 8.70 (brs, 1H).

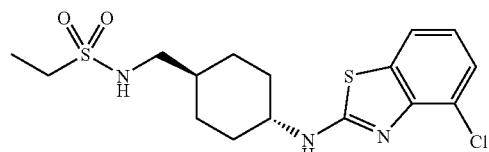
55



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1H-NMR (DMSO-d₆) δ: 0.92-1.15 (m, 2H), 1.15-1.35 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.33-1.48 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.78-2.84 (m, 2H), 2.97 (q, 2H, J=7.2 Hz), 3.62-3.80 (m, 1H), 7.02 (t, 1H, J=6.0 Hz), 7.45 (d, 1H, J=9.0 Hz), 8.09 (dd, 1H, J=9.0, 2.4 Hz), 8.68 (d, 1H, J=2.4 Hz), 8.70 (brs, 1H).

[Formula 499]



65

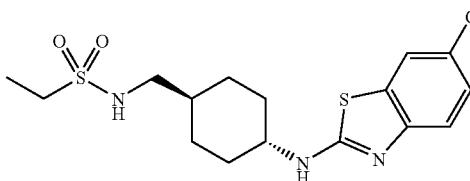
1H-NMR (DMSO-d₆) δ: 1.02-1.08 (m, 2H), 1.17-1.29 (m, 2H), 1.19 (t, 3H, J=7.5 Hz), 1.36-1.43 (m, 1H), 1.79-1.85 (m, 2H), 2.05-2.11 (m, 2H), 2.79 (t, 2H, J=6.0 Hz), 2.99 (q, 2H, J=7.5 Hz), 3.53-3.62 (m, 1H), 6.98 (t, 1H, J=7.8 Hz), 7.03 (t, 1H, J=6.3 Hz), 7.28 (dd, 1H, J=7.5, 1.2 Hz), 7.63 (dd, 1H, J=7.5, 1.2 Hz), 8.28 (d, 1H, J=7.5 Hz).

Compound Ij-127

448

1H-NMR (DMSO-d₆) δ: 1.02-1.08 (m, 2H), 1.17-1.29 (m, 2H), 1.19 (t, 3H, J=7.5 Hz), 1.36-1.43 (m, 1H), 1.79-1.85 (m, 2H), 2.05-2.11 (m, 2H), 2.79 (t, 2H, J=6.0 Hz), 2.99 (q, 2H, J=7.5 Hz), 3.53-3.62 (m, 1H), 6.98 (t, 1H, J=7.8 Hz), 7.03 (t, 1H, J=6.3 Hz), 7.28 (dd, 1H, J=7.5, 1.2 Hz), 7.63 (dd, 1H, J=7.5, 1.2 Hz), 8.28 (d, 1H, J=7.5 Hz).

[Formula 500]

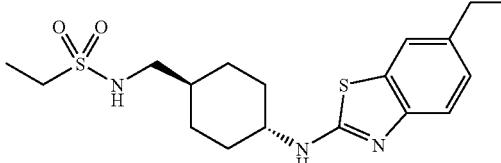


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1H-NMR (DMSO-d₆) δ: 0.97-1.05 (m, 2H), 1.18-1.24 (m, 2H), 1.16 (t, 3H, J=7.5 Hz), 1.34-1.41 (m, 1H), 1.77-1.81 (m, 2H), 2.02-2.08 (m, 2H), 2.76 (t, 2H, J=6.0 Hz), 2.96 (q, 2H, J=7.5 Hz), 3.55-3.64 (m, 1H), 7.00 (t, 1H, J=7.8 Hz), 7.18 (dd, 1H, J=8.4, 1.8 Hz), 7.32 (dd, 1H, J=8.4, 0.6 Hz), 7.74 (d, 1H, J=1.8 Hz), 8.04 (d, 1H, J=7.8 Hz).

Compound Ij-128

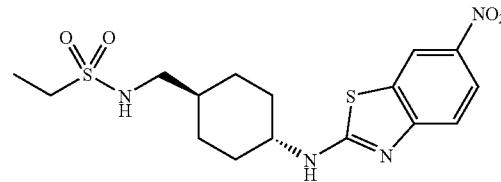
[Formula 501]



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1H-NMR (DMSO-d₆) δ: 0.98-1.07 (m, 2H), 1.15-1.26 (m, 8H), 1.32-1.43 (m, 1H), 1.78-1.84 (m, 2H), 1.98-2.09 (m, 2H), 2.60 (q, 2H, J=7.5 Hz), 2.78 (t, 2H, J=6.3 Hz), 2.96 (q, 2H, J=7.5 Hz), 3.55-3.64 (m, 1H), 6.98-7.05 (m, 2H), 7.27 (dd, 1H, J=7.8, 1.8 Hz), 7.47 (m, 1H), 7.84 (d, 1H, J=7.5 Hz).

[Formula 502]



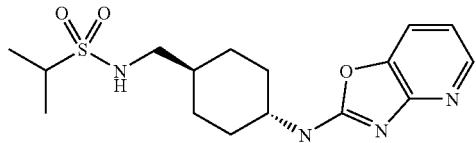
40

1H-NMR (DMSO-d₆) δ: 0.92-1.15 (m, 2H), 1.15-1.35 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.33-1.48 (m, 1H), 1.78-1.88 (m, 2H), 2.04-2.16 (m, 2H), 2.78-2.84 (m, 2H), 2.97 (q, 2H, J=7.2 Hz), 3.62-3.80 (m, 1H), 7.02 (t, 1H, J=6.0 Hz), 7.45 (d, 1H, J=9.0 Hz), 8.09 (dd, 1H, J=9.0, 2.4 Hz), 8.68 (d, 1H, J=2.4 Hz), 8.70 (brs, 1H).

449

Compound Ij-130

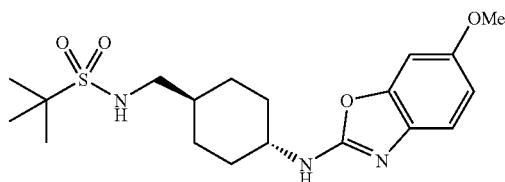
[Formula 503]

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¹H-NMR (DMSO-d₆) δ: 0.88-1.10 (m, 2H), 1.15-1.46 (m, 3H), 1.21 (d, 6H, J=6.6 Hz), 1.78-1.88 (m, 2H), 1.98-2.08 (m, 2H), 2.76-2.86 (m, 2H), 3.10-3.20 (m, 1H), 3.46-3.62 (m, 1H), 6.91-6.96 (m, 1H), 7.01 (brs, 1H), 7.64 (d, 1H, J=7.8 Hz), 8.07 (d, 1H, J=5.1 Hz), 8.35 (d, 1H, J=7.8 Hz).

Compound Ij-131

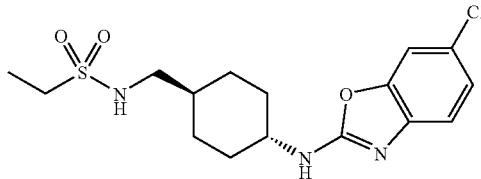
[Formula 504]

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¹H-NMR (DMSO-d₆) δ: 0.92-1.05 (m, 2H), 1.15-1.30 (m, 2H), 1.27 (s, 9H), 1.30-1.43 (m, 1H), 1.77-1.86 (m, 2H), 1.98-2.08 (m, 2H), 2.86-2.92 (m, 2H), 3.35-3.50 (m, 1H), 3.73 (s, 3H), 6.69 (dd, 1H, J=8.4, 2.0 Hz), 6.86 (t, 1H, J=6.0 Hz), 7.01 (d, 1H, J=2.0 Hz), 7.10 (d, 1H, J=8.4 Hz), 7.62 (d, 1H, J=7.6 Hz).

Compound Ij-132

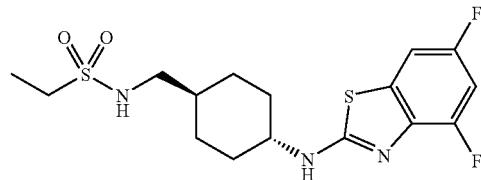
[Formula 505]

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¹H-NMR (DMSO-d₆) δ: 0.92-1.08 (m, 2H), 1.15-1.33 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.33-1.42 (m, 1H), 1.76-1.86 (m, 2H), 1.98-2.08 (m, 2H), 2.76-2.82 (m, 2H), 2.97 (q, 2H, J=7.2 Hz), 3.40-3.58 (m, 1H), 7.01 (t, 1H, J=6.0 Hz), 7.13 (d, 1H, J=8.4 Hz), 7.20 (d, 1H, J=8.4 Hz), 7.49 (s, 1H), 8.01 (d, 1H, J=7.6 Hz).

Compound Ij-133

[Formula 506]

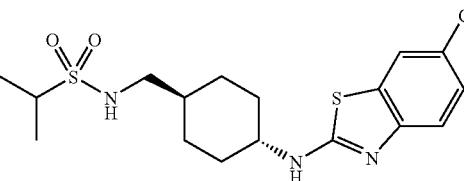
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¹H-NMR (DMSO-d₆) δ: 0.96-1.10 (m, 2H), 1.16-1.28 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.33-1.46 (m, 1H), 1.78-1.85 (m, 2H), 2.04-2.12 (m, 2H), 2.76-2.82 (m, 2H), 2.98 (q, 2H, J=7.2 Hz), 3.55-3.70 (m, 1H), 7.01 (t, 1H, J=6.0 Hz), 7.12 (t, 1H, J=9.6 Hz), 7.48 (d, 1H, J=7.6 Hz), 8.13 (d, 1H, J=7.6 Hz).

450

Compound Ij-134

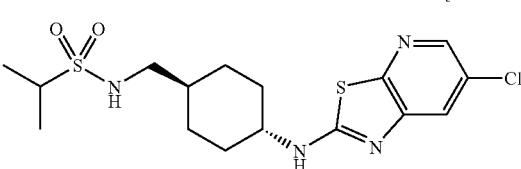
[Formula 507]

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¹H-NMR (DMSO-d₆) δ: 0.98-1.08 (m, 2H), 1.15-1.26 (m, 2H), 1.21 (d, 6H, J=6.9 Hz), 1.33-1.42 (m, 1H), 1.39-1.84 (m, 2H), 2.05-2.09 (m, 2H), 2.81 (t, 2H, J=6.3 Hz), 3.10-3.20 (m, 1H), 3.61-3.75 (m, 1H), 6.98 (t, 1H, J=6.0 Hz), 7.45 (dd, 1H, J=7.5, 0.6 Hz), 7.60 (dd, 1H, J=8.4, 1.5 Hz), 8.17 (d, 1H, J=1.5 Hz), 8.50 (d, 1H, J=7.5 Hz).

Compound Ij-135

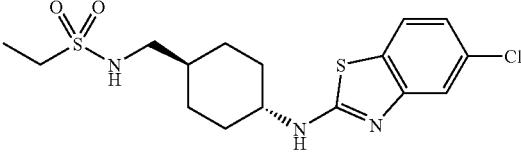
[Formula 508]

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¹H-NMR (DMSO-d₆) δ: 0.98-1.08 (m, 2H), 1.15-1.25 (m, 2H), 1.21 (d, 6H, J=6.6 Hz), 1.35-1.44 (m, 1H), 1.80-1.84 (m, 2H), 2.05-2.08 (m, 2H), 2.81 (t, 2H, J=6.3 Hz), 3.10-3.19 (m, 1H), 3.62-3.78 (m, 1H), 6.98 (t, 1H, J=6.0 Hz), 7.79 (d, 1H, J=2.1 Hz), 8.10 (d, 1H, J=2.1, 1.5 Hz), 8.52 (d, 1H, J=6.9 Hz).

Compound Ij-136

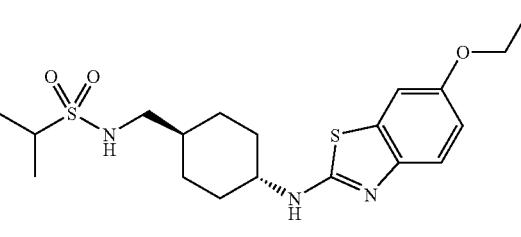
[Formula 509]

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¹H-NMR (DMSO-d₆) δ: 0.97-1.08 (m, 2H), 1.17-1.24 (m, 2H), 1.19 (t, 3H, J=7.5 Hz), 1.33-1.41 (m, 1H), 1.78-1.83 (m, 2H), 2.04-2.08 (m, 2H), 2.78 (t, 2H, J=6.3 Hz), 2.98 (q, 2H, J=7.2 Hz), 3.56-3.67 (m, 1H), 7.00-7.04 (m, 2H), 7.39 (d, 1H, J=2.1 Hz), 7.66 (dd, 1H, J=8.4, 1.8 Hz), 8.14 (d, 1H, J=7.5 Hz).

Compound Ij-137

[Formula 510]

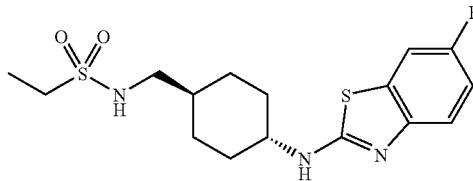
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¹H-NMR (DMSO-d₆) δ: 0.96-1.10 (m, 2H), 1.12-1.28 (m, 2H), 1.21 (d, 6H, J=6.9 Hz), 1.31 (t, 3H, J=6.9 Hz), 1.33-1.46 (m, 1H), 1.76-1.85 (m, 2H), 2.02-2.16 (m, 2H), 2.78-2.84 (m, 2H), 3.10-3.22 (m, 1H), 3.50-3.64 (m, 1H), 3.98 (q, 2H, J=6.9 Hz), 6.78 (dd, 1H, J=8.7, 2.7 Hz), 6.98 (t, 1H, J=6.0 Hz), 7.23-7.27 (m, 2H), 7.68 (d, 1H, J=7.2 Hz).

451

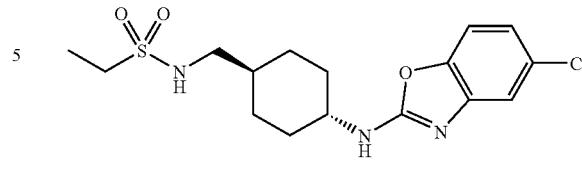
Compound Ij-138

[Formula 511]

**452**

Compound Ij-142

[Formula 515]

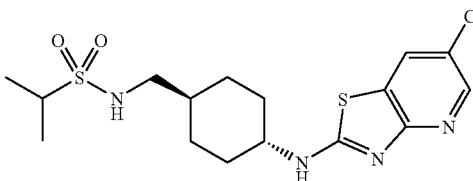


1H-NMR (DMSO-d₆) δ: 0.94-1.08 (m, 2H), 1.14-1.26 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.33-1.45 (m, 1H), 1.77-1.86 (m, 2H), 2.03-2.12 (m, 2H), 2.76-2.82 (m, 2H), 2.98 (q, 2H, J=7.2 Hz), 3.52-3.68 (m, 1H), 6.97-7.06 (m, 2H), 7.34 (dd, 1H, J=8.4, 4.8 Hz), 7.56 (dd, 1H, J=8.4, 2.4 Hz), 7.91 (d, 1H, J=7.6 Hz).

1H-NMR (DMSO-d₆) δ: 0.94-1.06 (m, 2H), 1.17-1.30 (m, 2H), 1.18 (t, 3H, J=7.5 Hz), 1.32-1.41 (m, 1H), 1.79-1.84 (m, 2H), 2.01-2.05 (m, 2H), 2.77 (t, 2H, J=6.0 Hz), 2.98 (q, 2H, J=7.2 Hz), 3.41-3.58 (m, 1H), 6.97 (dd, 1H, J=8.4, 2.4 Hz), 6.99-7.03 (m, 1H), 7.27 (d, 1H, J=2.4 Hz), 7.34 (dd, 1H, J=8.4, 0.3 Hz), 8.07-8.14 (m, 1H).

Compound Ij-139

[Formula 512]

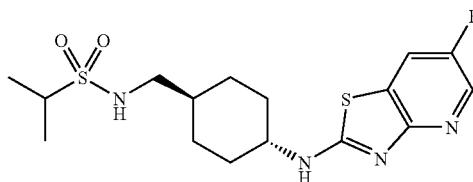


1H-NMR (DMSO-d₆) δ: 0.96-1.12 (m, 2H), 1.16-1.32 (m, 2H), 1.21 (d, 6H, J=6.6 Hz), 1.32-1.46 (m, 1H), 1.78-1.86 (m, 2H), 2.02-2.16 (m, 2H), 2.78-2.84 (m, 2H), 3.10-3.21 (m, 1H), 3.58-3.76 (m, 1H), 7.00 (t, 1H, J=6.0 Hz), 8.19-8.23 (m, 2H), 8.52 (d, 1H, J=6.9 Hz).

1H-NMR (DMSO-d₆) δ: 0.94-1.08 (m, 2H), 1.16-1.33 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.33-1.45 (m, 1H), 1.77-1.86 (m, 2H), 2.00-2.08 (m, 2H), 2.74-2.82 (m, 2H), 2.98 (q, 2H, J=7.2 Hz), 3.38-3.54 (m, 1H), 6.90-7.00 (m, 1H), 7.02 (t, 1H, J=4.5 Hz), 7.19 (dd, 1H, J=8.4, 5.1 Hz), 7.33 (dd, 1H, J=8.4, 2.7 Hz), 7.88 (d, 1H, J=7.8 Hz).

Compound Ij-140

[Formula 513]

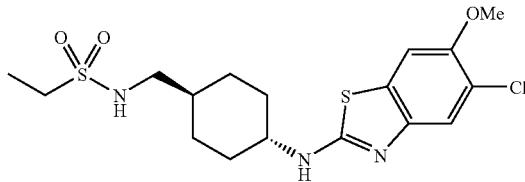


1H-NMR (DMSO-d₆) δ: 0.96-1.12 (m, 2H), 1.12-1.30 (m, 2H), 1.21 (d, 6H, J=6.6 Hz), 1.32-1.46 (m, 1H), 1.78-1.86 (m, 2H), 2.02-2.16 (m, 2H), 2.78-2.84 (m, 2H), 3.10-3.20 (m, 1H), 3.58-3.78 (m, 1H), 7.01 (t, 1H, J=6.0 Hz), 8.08 (dd, 1H, J=8.4, 2.7 Hz), 8.19 (d, 1H, J=2.7 Hz), 8.38 (d, 1H, J=7.2 Hz).

1H-NMR (DMSO-d₆) δ: 0.94-1.06 (m, 2H), 1.19-1.29 (m, 2H), 1.18 (t, 3H, J=7.2 Hz), 1.31-1.41 (m, 1H), 1.79-1.84 (m, 2H), 2.01-2.05 (m, 2H), 2.77 (t, 2H, J=6.0 Hz), 2.98 (q, 2H, J=6.9 Hz), 3.41-3.57 (m, 1H), 6.71-6.79 (m, 1H), 7.06-7.08 (m, 2H), 7.31 (dd, 1H, J=8.7, 4.8 Hz), 8.03 (d, 1H, J=7.8 Hz).

Compound Ij-141

[Formula 514]



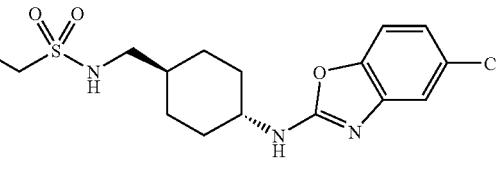
1H-NMR (DMSO-d₆) δ: 0.97-1.08 (m, 2H), 1.15-1.22 (m, 5H), 1.34-1.42 (m, 1H), 1.78-1.83 (m, 2H), 2.04-2.08 (m, 2H), 2.78 (t, 2H, J=6.0 Hz), 2.98 (q, 2H, J=7.2 Hz), 3.53-3.62 (m, 1H), 3.81 (s, 1H), 7.02 (t, 1H, J=6.3 Hz), 7.41 (s, 1H), 7.53 (s, 1H), 7.88 (d, 1H, J=7.5 Hz).

1H-NMR (DMSO-d₆) δ: 0.95-1.16 (m, 2H), 1.18-1.44 (m, 3H), 1.21 (d, 6H, J=6.6 Hz), 1.78-1.86 (m, 2H), 2.02-2.12 (m, 2H), 2.78-2.84 (m, 2H), 3.10-3.20 (m, 1H), 3.40-3.58 (m, 1H), 6.95 (t, 1H, J=7.8 Hz), 7.01 (brs, 1H), 7.09 (t, 1H, J=6.9 Hz), 7.22 (d, 1H, J=6.6 Hz), 7.31 (d, 1H, J=7.8 Hz), 7.83 (d, 1H, J=7.8 Hz).

452

Compound Ij-142

[Formula 515]

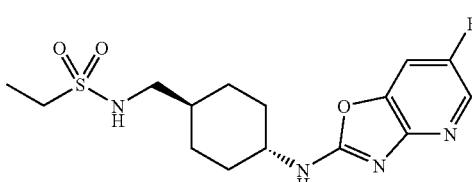


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1H-NMR (DMSO-d₆) δ: 0.94-1.06 (m, 2H), 1.17-1.30 (m, 2H), 1.18 (t, 3H, J=7.5 Hz), 1.32-1.41 (m, 1H), 1.79-1.84 (m, 2H), 2.01-2.05 (m, 2H), 2.77 (t, 2H, J=6.0 Hz), 2.98 (q, 2H, J=7.2 Hz), 3.41-3.58 (m, 1H), 6.97 (dd, 1H, J=8.4, 2.4 Hz), 6.99-7.03 (m, 1H), 7.27 (d, 1H, J=2.4 Hz), 7.34 (dd, 1H, J=8.4, 0.3 Hz), 8.07-8.14 (m, 1H).

Compound Ij-143

[Formula 516]



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1H-NMR (DMSO-d₆) δ: 0.94-1.08 (m, 2H), 1.16-1.33 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.33-1.45 (m, 1H), 1.77-1.86 (m, 2H), 2.00-2.08 (m, 2H), 2.74-2.82 (m, 2H), 2.98 (q, 2H, J=7.2 Hz), 3.38-3.54 (m, 1H), 6.90-7.00 (m, 1H), 7.02 (t, 1H, J=4.5 Hz), 7.19 (dd, 1H, J=8.4, 5.1 Hz), 7.33 (dd, 1H, J=8.4, 2.7 Hz), 7.88 (d, 1H, J=7.8 Hz).

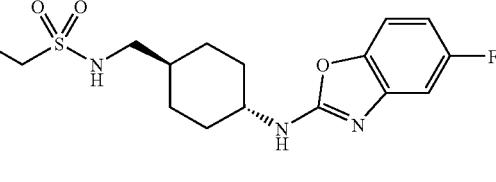
25

1H-NMR (DMSO-d₆) δ: 0.94-1.08 (m, 2H), 1.16-1.33 (m, 2H), 1.19 (t, 3H, J=7.2 Hz), 1.33-1.45 (m, 1H), 1.77-1.86 (m, 2H), 2.00-2.08 (m, 2H), 2.74-2.82 (m, 2H), 2.98 (q, 2H, J=7.2 Hz), 3.38-3.54 (m, 1H), 6.90-7.00 (m, 1H), 7.02 (t, 1H, J=4.5 Hz), 7.19 (dd, 1H, J=8.4, 5.1 Hz), 7.33 (dd, 1H, J=8.4, 2.7 Hz), 7.88 (d, 1H, J=7.8 Hz).

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Compound Ij-144

[Formula 517]



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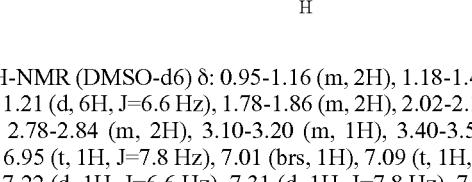
1H-NMR (DMSO-d₆) δ: 0.94-1.06 (m, 2H), 1.19-1.29 (m, 2H), 1.18 (t, 3H, J=7.2 Hz), 1.31-1.41 (m, 1H), 1.79-1.84 (m, 2H), 2.01-2.05 (m, 2H), 2.77 (t, 2H, J=6.0 Hz), 2.98 (q, 2H, J=6.9 Hz), 3.41-3.57 (m, 1H), 6.71-6.79 (m, 1H), 7.06-7.08 (m, 2H), 7.31 (dd, 1H, J=8.7, 4.8 Hz), 8.03 (d, 1H, J=7.8 Hz).

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1H-NMR (DMSO-d₆) δ: 0.94-1.06 (m, 2H), 1.19-1.29 (m, 2H), 1.18 (t, 3H, J=7.2 Hz), 1.31-1.41 (m, 1H), 1.79-1.84 (m, 2H), 2.01-2.05 (m, 2H), 2.77 (t, 2H, J=6.0 Hz), 2.98 (q, 2H, J=6.9 Hz), 3.41-3.57 (m, 1H), 6.71-6.79 (m, 1H), 7.06-7.08 (m, 2H), 7.31 (dd, 1H, J=8.7, 4.8 Hz), 8.03 (d, 1H, J=7.8 Hz).

Compound Ij-145

[Formula 518]



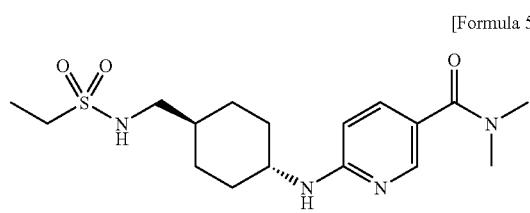
55

1H-NMR (DMSO-d₆) δ: 0.95-1.16 (m, 2H), 1.18-1.44 (m, 3H), 1.21 (d, 6H, J=6.6 Hz), 1.78-1.86 (m, 2H), 2.02-2.12 (m, 2H), 2.78-2.84 (m, 2H), 3.10-3.20 (m, 1H), 3.40-3.58 (m, 1H), 6.95 (t, 1H, J=7.8 Hz), 7.01 (brs, 1H), 7.09 (t, 1H, J=6.9 Hz), 7.22 (d, 1H, J=6.6 Hz), 7.31 (d, 1H, J=7.8 Hz), 7.83 (d, 1H, J=7.8 Hz).

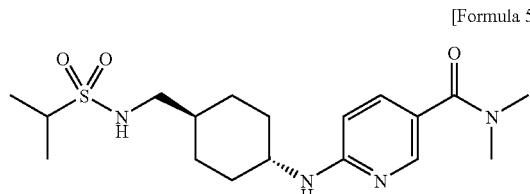
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453

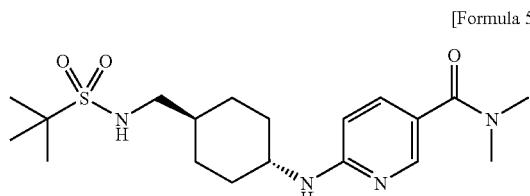
Compound Ij-146



Compound Ij-147



Compound Ij-148



Experiment 1

Transportability Through the Blood-Brain Barrier and Potential for Drug-Drug Interactions Through P-gp

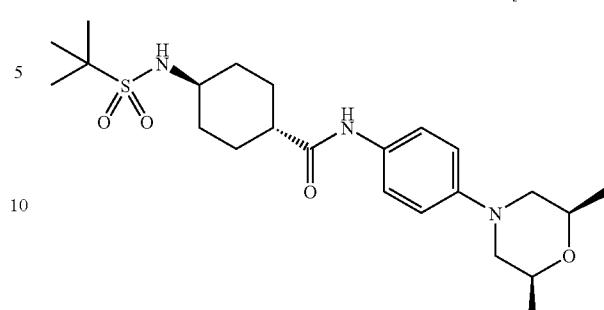
Transportability of the compounds of the present invention through the blood-brain barrier (blood-brain partition coefficient; K_p) in mice (Jcl; C57BL/6J mice, ♂, 7 weeks) was defined from the difference in concentration of the compounds between in plasma and in brain after intravenous administration of the compounds (0.5 mg/2 mL/kg). The brain K_p value of Compound (I-72) ($K_{p,CSA}$) was 1.29 showing high transportability through the blood-brain barrier.

To examine the potential for drug-drug interactions through P-gp in vivo, the K_p values of compounds of the present invention with ($K_{p,CSA}$) or without ($K_{p,Cont.}$) cyclosporin A (20 mg/kg), a P-gp inhibitor, were calculated. The $K_{p,CSA}$ value of Compound (I-72) was 1.14, and the calculated $K_{p,CSA}/K_{p,Cont.}$ ratio was 0.9. The result indicate that Compound (I-72) has no significant potential for drug-drug interactions through P-gp in mice.

On the other hand the potential for drug-drug interactions through P-gp of amide compound B which has similar structure of Compound (I-72) was also examined in mice. The $K_{p,Cont.}$ and $K_{p,CSA}$ were 0.04 and 0.84, respectively. The $K_{p,CSA}/K_{p,Cont.}$ ratio was more than 1.0 (i.e. 20.5), indicating that the compound is effectively excreted through P-gp from the brain to vessels, and that significant drug-drug interactions through P-gp could be induced in mice.

454

[Formula 522]



Compound B

Experiment 3

Inhibitory Effect on cAMP Production in CHO Cells

CHO cells expressing human NPY Y5 receptor were incubated in the presence of 2.5 mM isobutylmethylxanthine (SIGMA) at 37° C. for 20 min. After the incubation the compound of the present invention was added, and then the mixture was incubated for 5 min. Next, 50 nM NPY and 10 μM forskolin (SIGMA) were added, and the mixture was incubated for 30 min. After termination of the reaction by adding 1N HCl, the amount of cAMP in the supernatant was determined with an EIA kit (Amersham LIFE SCIENCE). The inhibitory activity of NPY against forskolin stimulated cAMP production was expressed as 100% and the 50% inhibitory concentration (IC₅₀ value) of the compound of the present invention against the NPY activity was calculated.

Experiment 4

Using the membranes prepared from Y1-expression cells (human neuroblastoma, SK-N-MC) and the membranes prepared from Y2-expression cells (human neuroblastoma, SMS-KAN), the experiment was carried out in a similar way as Experiment 2 to determine the affinity of the compounds for NPY Y1 and NPY Y2 receptor. The results showed that the compounds of the present invention had no significant affinity for their receptors, indicating high selectivity for NPY Y5 receptor.

Experiment 5

Under diethylether anesthesia the skull of male C57BL/6J mice (12-14 week old, 25-30 g) was exposed by making an incision about 1-cm long from external occipital crest to nasal dorsum, and drilled in the 1-mm lateral position to the left following 1-mm posterior from bregma. After recovery from anesthesia mice were dosed with either 0.5% hydroxypropylmethyl cellulose solution (Shin-Etsu Chemical Co., Ltd) or the compounds of the present invention suspended in the 0.5% hydroxypropylmethyl cellulose solution. At one hour after the treatment, each animal received a NPY Y5 receptor specific agonist, [cPP1-7, NPY19-23, A1a31, Aib32, Gln34]-hPancreatic Polypeptide (0.1 nmol/1.5 μL/mouse) through the skull opening using a canula. Residual food was measured at 2 and 4 hours after the treatment, and the difference in food intake between the compounds-treated mice and 0.5% hydroxypropylmethyl cellulose solution-treated mice was calculated. The compound at 6 mg/kg caused a significant

455

reduction in food intake of mice compared to the treatment with 0.5% hydroxypropylmethyl cellulose solution.

Formulation Example

The following Formulation Examples are only exemplified and not intended to limit the scope of the present invention.

Formulation Example 1**Tablets**

Compound (I-1)	15 mg
Starch	15 mg
Lactose	15 mg
Crystalline cellulose	19 mg
Polyvinyl alcohol	3 mg
Distilled water	30 ml
Calcium stearate	3 mg

All of the above ingredients except for calcium stearate are uniformly mixed. Then the mixture was crushed, granulated and dried to obtain a suitable size of granules. Next, calcium stearate was added to the granules. Finally, tabletting was performed under a compression force.

Formulation Example 2**Capsules**

Compound (I-2)	10 mg
Magnesium stearate	10 mg
Lactose	80 mg

The above ingredients were mixed uniformly to obtain powders or fine granules, and then the obtained mixture was filled in capsules.

Formulation Example 3**Granules**

Compound (I-3)	30 g
Lactose	265 g
Magnesium Stearate	5 g

After the above ingredients are mixed uniformly, the mixture was compressed. The compressed matters were crushed, granulated and sieved to obtain suitable size of granules.

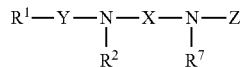
INDUSTRIAL APPLICABILITY

As shown in the above Experiments, the compounds of the present invention have a NPYY5 receptor antagonistic activity. Therefore, the compounds of the present invention are very useful as an anti-obesity and anorectic agent.

456

The invention claimed is:

1. A compound of a formula:

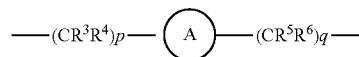


or

a pharmaceutically acceptable salt thereof,
wherein

R1 is optionally substituted lower alkyl,
Y is $-S(O)2-$,

R2 is hydrogen or optionally substituted lower alkyl,
R7 is hydrogen or optionally substituted lower alkyl,
X is a group of a formula:



wherein R3 and R4 are each independently hydrogen,
a group of a formula:



is optionally substituted 1,4-cyclohexanediyl,
p is 1 or 2,

q is 0, and

provided that a group of a formula:

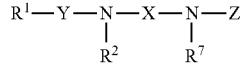


is not a group of a formula:



wherein R14 is optionally substituted phenyl, and
Z is optionally substituted phenyl, optionally substituted
quinolyl, optionally substituted isoquinolyl, optionally
substituted benzothiazolyl, optionally substituted benz-
imidazolyl, optionally substituted benzoxazolyl, option-
ally substituted thiazolopyridyl, optionally substituted
oxazolopyridyl or optionally substituted pyrazolyl.

2. A compound of a formula:



or

a pharmaceutically acceptable salt thereof,
wherein

R1 is optionally substituted lower alkyl,
Y is $-S(O)2-$,

457

R₂ is hydrogen or optionally substituted lower alkyl,
R₇ is hydrogen or optionally substituted lower alkyl,
X is a group of a formula:



wherein R₃ and R₄ are each independently hydrogen, a group of a formula:



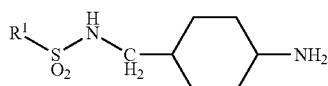
is optionally substituted 1,4-cyclohexanediyl,
p is 1 or 2, and

q is 0, and

Z is optionally substituted phenyl, optionally substituted quinolyl, optionally substituted isoquinolyl, optionally substituted benzothiazolyl, optionally substituted benzimidazolyl, optionally substituted benzoxazolyl, optionally substituted thiazolopyridyl, optionally substituted oxazolopyridyl or optionally substituted pyrazolyl.

3. A pharmaceutical composition comprising the compound or the pharmaceutically acceptable salt thereof according to claim 1 or 2 as an active ingredient.

4. A compound of a formula:

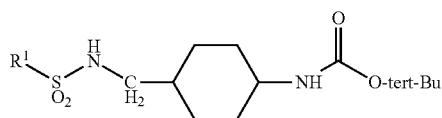


or

a salt thereof,

wherein R₁ is ethyl or tert-butyl.

5. A compound of a formula:

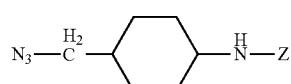


or

a salt thereof,

wherein R₁ is ethyl, isopropyl or tert-butyl.

6. A compound of a formula:



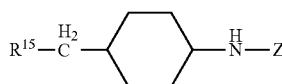
or

a salt thereof,

wherein Z is optionally substituted carbocyclyl or optionally substituted heterocyclyl.

458

7. A compound of a formula:



or

a salt thereof,

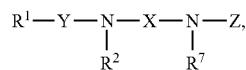
wherein

R_{1᳚} is NH₂ or OH, and

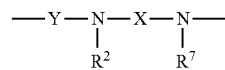
Z is optionally substituted pyridazinyl, optionally substituted pyrazinyl, optionally substituted quinolyl, optionally substituted isoquinolyl, optionally substituted benzothiazolyl, optionally substituted benzoxazolyl, optionally substituted benzopyridyl, optionally substituted benzopyridazinyl, optionally substituted benzoxazolyl, optionally substituted thiazolopyridyl, optionally substituted benzisoxazolinonyl, optionally substituted benzoxazolinonyl, optionally substituted benzoxadionyl or optionally substituted benzoxyazepinonyl.

8. The compound or the pharmaceutically acceptable salt thereof according to claim 1, wherein R₁ is optionally substituted C₂ to C₁₀ alkyl.

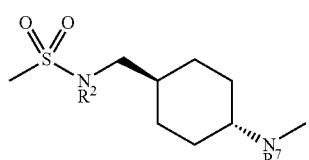
9. The compound or the pharmaceutically acceptable salt thereof according to claim 1, wherein in the formula of



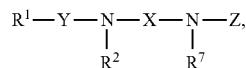
35 a group of formula:



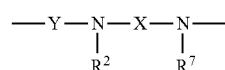
40 corresponds to



45 **10.** The compound or the pharmaceutically acceptable salt thereof according to claim 1, wherein in the formula of



55 a group of formula:



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a salt thereof,

wherein Z is optionally substituted carbocyclyl or optionally substituted heterocyclyl.

US 9,150,507 B2

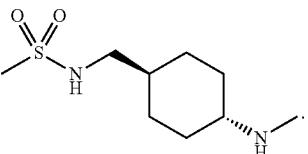
459

corresponds to

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* * * *